

# American Journal of Obstetrics and Gynecology

VOL. 28

ST. LOUIS, AUGUST, 1934

No. 2

## Original Communications

### THE TREATMENT OF DYSMENORRHEA BY RESECTION OF THE PRESACRAL SYMPATHETIC NERVES: EVALUATION OF END-RESULTS\*

VIRGIL S. COUNSELLER, M.D., AND WINCHELL MCK. CRAIG, M.D.,  
ROCHESTER, MINN.

*(From the Division of Surgery and Section on Neurologic Surgery, The Mayo Clinic)*

#### GENERAL CONSIDERATIONS OF DYSMENORRHEA

DYSMENORRHEA is divided into two types; the first is designated as essential or primary dysmenorrhea, and the second as secondary dysmenorrhea, since it is associated with other demonstrable pelvic pathologic change, such as uterine myoma, endometriosis, salpingitis, ovarian tumors, and displacements. The latter is characterized during menstruation, by increased discomfort and other subjective symptoms, which usually subside when the period of flow is over. Surgical removal of the diseased organs, and correction of malpositions of the uterus is all that is essential for satisfactory relief.

Primary dysmenorrhea, on the other hand, is not dependent on pelvic pathologic change, but may be associated with it. Usually the pelvic organs appear normal, and for this reason it is essential carefully to analyze each patient in order to apply the correct surgical treatment. Primary dysmenorrhea has been one of the most difficult conditions which the gynecologist has had to treat; that is evidenced by the fact that many forms of treatment have been advocated. The cause of the

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NOTE: The Editor accepts no responsibility for the views and statements of authors as published in their "Original Communications."

\*Read before the meeting of the New York Obstetrical Society, New York City, New York, December 12, 1933.

condition still remains unknown; many hypotheses have been advanced. Among these was the hypothesis that displacements of the uterus caused menstrual blood to be retained within the uterus, and that the pain was incident to contractions of the uterus in an attempt to expel its content. The error of this theory is shown by the fact that in many instances of primary dysmenorrhea the cervix is easily dilated and that sounds can be passed without meeting any obstruction. Furthermore, Novak pointed out that the rate of discharge of menstrual blood by the normal woman averages only about two-thirds of a drop per minute, and it is difficult to believe that displacements could produce sufficient obstruction to interfere with the exit of such small amounts. Notwithstanding these facts, it is well known that ante flexion and retro flexion, associated with marked congestion at menstruation, are productive of some discomfort which, moreover, varies in degree and in many instances is benefited by correction of the displacements.

The hypothesis has been offered that hypoplasia of the pelvic organs, particularly of the uterus, is the chief cause of the pain. It was thought that the uterus was faulty in muscular development and could not respond normally to the menstrual stimulation. The principal obstacle to adoption of such a view is that in many instances of essential dysmenorrhea, the uterus is normal in size and consistency, and the dysmenorrhea is an acquired condition; almost 50 per cent of the patients relate that they menstruated normally for months or years following puberty, after which severe dysmenorrhea occurred.

Although many cases of dysmenorrhea can be explained on the basis of constitutional inferiority, neurosis, or psychoneurosis, not infrequently patients become neurotic secondarily as a result of monthly attacks of intolerable pain. Yet, there is no question that often constitutional or nervous instability results in a lower threshold for pain. In such instances, the slight discomfort associated with normal menstruation might be perceived as a severe disabling pain. According to Miller, it is easy to comprehend that repeated, periodic attacks of suffering are bound to exert a deleterious effect on the soundest of nervous systems, and that, as time goes on, the exhaustion from each period will last longer and the recovery from it will be less prompt. A vicious circle thus is ultimately set up; each succeeding period is harder to endure than the last, and recovery is more difficult. Furthermore, Miller reported that the majority of patients who seek relief from dysmenorrhea are in fairly good health. They have no special nervous symptoms, but are partially or entirely incapacitated for a certain period each month. In such cases the hypothesis that dysmenorrhea is of neurotic origin should not be lightly applied. Nevertheless, many patients improve remarkably when general constitutional measures are applied, together with careful and tactful analysis of the mental attitude of the patient toward her condition.



The relationship of endocrine dysfunction to dysmenorrhea has received much attention recently. That such dysfunction does exert definite influence cannot be denied. Knowledge of endocrine function at present is so limited, and the interrelation of the ovary, pituitary body, thyroid gland and suprarenal gland so definitely proved experimentally, that little evidence of clinical value can be related. The work of Novak and Reynolds in this field, however, is promising. On the basis of their experiments on animals, they have contended that whatever the primary cause of dysmenorrhea may be, the actual pain results from spasmodic contraction of the uterine muscle, and that the rhythmic uterine contractions exhibit definite variations which may be associated with the various sexual states and are definitely related to the various phases of endocrine activity. The rhythmic uterine contractions were shown to be the result of the ovarian follicular hormone which in crystalline form is known as theelin, and of it alone, whereas progesterin was shown to decrease or eliminate the contractions. The inhibition of uterine motility was similarly produced by injection of prolactin, which is derived from the urine of pregnant women, and which demonstrates the abundance of the inhibiting substance in the blood stream during pregnancy. Novak and Reynolds concluded, from these observations, that primary dysmenorrhea has its origin in exaggerated and spasmodic uterine contractions, and that these are the result of diminishing action of the corpus luteum and increasing action of folliculin, while this action is, in turn, inhibited by the action of progesterin. Withdrawal of the restraining factor produces dysmenorrhea of some women who have a lowered threshold for pain, whereas, with others, it would seem that there is an actual unbalance between the ovarian follicular hormone and progesterin, either quantitative, chronologic, or both.

Other investigators have considered the severe uterine contractions in dysmenorrhea to be the result of a disturbance or unbalance in the pelvic sympathetic nerve plexus, resulting not only in dysfunction of the uterus but of the ovary as well. Considerable evidence that such is the case is the fact that in a high percentage of cases of primary dysmenorrhea, there is associated sclerocystic disease of the ovaries. It has been our observation that frequently the greater the disability from dysmenorrhea in the presence of a sound general and nervous condition, the greater is the sclerocystic disease of the ovaries, providing there is no other associated pathologic change in the uterus or ovaries. Ovarian dysfunction is, therefore, a logical sequel to the cystic disease and to the unbalance in the secretion of hormones.

#### RESECTION OF PRESACRAL NERVE

The treatment of dysmenorrhea by surgically interrupting the sympathetic innervation of the generative organs is not new. Thirty-six years ago Jaboulay attempted to relieve pelvic neuralgia by interrupting

the afferent pathways in the sacral sympathetic chain by a posterior approach. One year following publication of the report of his work, Ruggi advocated abdominal sympathectomy for functional disturbances of the female genital organs. He advised resection of the utero-ovarian plexus by the transperitoneal route. Complete relief of pain was obtained in some instances by both investigators, but the procedures were not well received by their colleagues, and the operation was soon discarded. Interest in the pelvic sympathetic nerves was revived, however, by Leriche,<sup>11</sup> in 1921. He advocated periarterial sympathectomy of the hypogastric artery as a means of relieving the pain in cases of functional dysmenorrhea. In a large majority of the cases, the results obtained by Cotte,<sup>4</sup> Michon,<sup>13</sup> and Leriche<sup>12</sup> were complete and lasting relief.

Periarterial sympathectomy was time-consuming and difficult, so that a more simplified technic, which would give the same beneficial results, was essential.

Such a procedure was advanced by Cotte<sup>3</sup> in 1925, and consisted of resection of the superior hypogastric plexus (presacral nerve). This has been the operation of choice for functional dysmenorrhea, but in cases in which the pain apparently involves all the pelvic viscera, Leriche<sup>12</sup> advocated that resection of the presacral nerves be combined with periarterial sympathectomy applied to the internal iliac artery. Cotte,<sup>5</sup> in 1927, reported good results in 90 cases and, in 1929,<sup>6</sup> reported 200 cases in which treatment by resection of the presacral nerves had given satisfactory results. Michon<sup>13</sup> reported complete relief of all subjective symptoms in 22 cases treated by a combination of presacral and periarterial sympathectomy. Cueille, in 1929, also reported that complete relief of the pelvic pain had resulted from resection of the presacral nerves in 12 cases. Fontaine and Herrmann obtained excellent results with 13 of 15 patients whom they were able to follow by questionnaires. Other foreign surgeons have confirmed these results, while Adson and Masson in this country likewise obtained nearly complete relief in their 6 cases.

A number of cases of dysmenorrhea have now been treated by resection of the superior hypogastric plexus, and the reported results have been such that the procedure has been definitely established as part of the treatment of obstinate and painful menstruation. The excellent results in the surgical treatment of Raynaud's disease, scleroderma, thrombo-angiitis obliterans, and various degrees of arthritis, by sympathetic ganglionectomy and trunk resection have further served to stimulate interest in the application of sympathectomy in treatment of primary or essential dysmenorrhea on the basis that these conditions are manifestations of ovarian or uterine dysfunction.

At the Mayo Clinic, resection of the presacral nerve has been performed in 14 cases of dysmenorrhea. In all cases in which any associated pelvic pathologic condition was noted it was corrected at the same operation.

#### REPORT OF CASES

CASES 1 TO 6.—These cases were reported by Adson and Masson. We can add only one feature to their report concerning these six cases. Since they wrote their

report, the patient of their Case 6 has stated that she has remained free from dysmenorrhea and that her periods are normal.

CASE 7.—A married woman, aged twenty-seven years, came to the clinic because of menorrhagia and dysmenorrhea which had been increasing in severity for eighteen months. The menstrual periods had always been regular, occurring every twenty-four days, but had been associated with a moderate amount of dysmenorrhea. The woman had had one child. Eighteen months prior to registration, she had noticed that menstruation had become more painful and that flow was more profuse than formerly. Eight months previous to her coming to the clinic, the appendix and a portion of the right ovary had been removed, and diagnostic dilatation and curettage had been carried out and the perineum had been repaired. Recovery from the operation had been uneventful, but the pain in the lower part of the abdomen had recurred, and had been associated with more dysmenorrhea. The pains in her back and abdomen had been so severe that she had been confined to bed for four or five days at each menstruation. There had been some dyspareunia in the past eight months.

On bimanual examination, the uterus was found to be about one and a half times the normal size, and movable in the anterior position. Both adnexa were moderately tender. The cervix was normal. The patient appeared markedly exhausted; she was somewhat obese, and was greatly depressed about her menses. No improvement was obtained from diagnostic dilatation and curettage and application of 400 mg. hr. of radium. Five months following these procedures, the patient returned to the clinic in exactly the same condition. Aug. 24, 1933, a few small cysts of the left ovary were resected, many pelvic adhesions were separated, and the hypogastric plexus was removed. The uterus was normal in size and was in good position. There was no disturbance of the urinary bladder.

Oct. 30, 1933, the patient wrote that her general health had gradually improved, and that she was able to do all of her own housework. Her periods were normal and she was completely relieved of pain.

CASE 8.—A married woman, aged thirty-one years, came to the clinic because of pain in the lower part of the abdomen, which she felt was definitely associated with menstruation. The pain had been somewhat localized in the left lower abdominal quadrant, and had been associated with some vesical discomfort. Six months after the onset, the severity of the pain had become that of typical labor. The pain had come on during menstruation, and had lasted throughout the period of flow. More recently, the same type of pain had been present almost daily, and the woman had required from one to two tablets of pantopon per day, for relief. The pain often had been aggravated by defecation. Previously, the menstrual periods had always been regular, but during the last year the flow had lasted from ten days to three weeks. The patient had been twice pregnant, and during both pregnancies, the first six years, and the second sixteen months before she came to the clinic, morphine had been required almost daily to control the labor pains in an attempt to prevent spontaneous abortion.

Examination disclosed some tenderness and fixation of the left adnexa. The uterus was of normal size but was in retroversion. Neurologic examination disclosed that the central system was essentially normal. Sept. 19, 1933, the left tube and ovary were removed because of chronic salpingo-oophoritis. The presacral nerve was then resected and intraperitoneal shortening of the round ligaments was performed.

The patient was completely relieved of the pain and received an excellent result from the operation. The menstrual flow was decreased.

CASE 9.—A married woman, aged twenty-six years, came to the clinic complaining of pain in the right lower abdominal quadrant, which had been accentuated during

menstruation, for the past six years. Her menses had begun at the age of fourteen years, had occurred every twenty-eight days, and flow had lasted four days, without pain. During the past six years, she said, she had experienced continual, dull discomfort in the right lower abdominal quadrant, associated with periodic exacerbations during, before, or after menstruation. The length of an attack was about twenty-four hours, during which time the pain was excruciating and was accompanied by nausea and vomiting. She was prostrate throughout the entire attack. If the attack preceded the onset of menstruation, the latter was likely to be mild. If it did not, there was marked dysmenorrhea. Occasionally, pain or discomfort was not present before menstruation, nor did either pain or discomfort appear at the onset of flow, but in such an instance, the pain usually came on two or three days after the onset of flow.

Feb. 25, 1933, a hemorrhagic cyst of the right ovary and a single adenomyoma of the right horn of the uterus were removed. About 3 cm. of the presacral nerve was then resected.

Convalescence was uneventful. In June, the patient reported that she was completely relieved of all of the discomfort associated with the menstrual period; also, that her general health was rapidly improving.

CASE 10.—A married woman, aged thirty-four years, came to the clinic complaining of severe dysmenorrhea which had been present for nine months. She had two children, aged fourteen and twelve years. The patient always had been well until nine months before her registration, when the menstrual flow had become very scanty and there had been associated cramps, which she had never had before; these occurred during the next three menses. Diagnostic dilatation and curettage had been performed, elsewhere, without benefit. About the same amount of flow and degree of dysmenorrhea had continued. Her general health was otherwise satisfactory, although she was extremely nervous and irritable, and cried easily.

Laparotomy was performed Sept. 7, 1933, when both ovaries were partially resected for cystic oophoritis. Tissue equal to about half of an ovary of normal size was saved on each side. The appendix was chronically diseased and was removed. Intraperitoneal shortening of the round ligaments was done after the modified Gilliam method, for retroversion, Grade 3. The presacral nerve was then resected.

In a communication from the patient, received October 24, she stated that she had had a normal menstrual period without pain and was feeling better than she had felt for years.

CASE 11.—A married woman, aged thirty-eight years, came to the clinic complaining of painful menstruation since its onset at the age of fourteen years. The periods had been regular, twenty-one to twenty-three days; flow had been moderate in amount and had lasted four days. At the beginning of the menses, she had had attacks of generalized abdominal colic, lasting from two to three days. Pain had been somewhat intermittent, coming every three to four hours and lasting fifteen to twenty minutes. In late years, menstruation had been associated with frontal headache, nausea, and vomiting. The patient was the mother of three living children and had had two miscarriages after three months' gestation. Pregnancies had had no influence on the degree of dysmenorrhea.

Aug. 16, 1933, the presacral nerves were resected. The uterus and adnexa were normal. Convalescence was uneventful and the wound healed by primary union. The patient had no pain during the first menses after operation, which occurred when she was in the hospital.

CASE 12.—A single woman, aged twenty-six years, came to the clinic complaining chiefly of painful menstruation; the pain had become much more severe in the three

years previous to her admission. Menses had begun at the age of fourteen years, occurred every twenty-eight days and lasted about five days. The pain had been confined to both iliac fossae, and to the sacrum and rectum posteriorly. It had been so severe that she had been compelled to go to bed for the first day or two and to take sodium iso-amylethyl barbiturate (sodium amytal).

In addition to the painful menstruation, there was a large element of fatigue, with nausea and lack of appetite; the patient seemed to be constitutionally inferior. Because of the dysmenorrhea, laparotomy was performed Aug. 11, 1933. There was a granulating area at the juncture of the left uterosacral ligament and the uterus; this was excised and proved to be endometrium. The presacral nerves were then resected.

In a report from the patient, received Nov. 18, 1933, she stated that she was completely relieved of all of the former pain, and that the periods were entirely normal.

CASE 13.—A single woman, aged thirty years, registered at the clinic complaining of dysmenorrhea, backache, and headache. She had always had painful menstruation, but it had gradually increased in severity until it had become intolerable. The pain radiated across the hips, down the thighs, and all over the lower part of the abdomen. It was much worse preceding the menses and then recurred for a few days after cessation of flow. Medication always had been required for the pain. Menses had occurred every three weeks and lasted for ten or twelve days. During the first half of the periods the flow had been very scanty, but during the last half it had been normal in amount. Ventral suspension of the uterus had been performed two years before her admission, with only moderate relief.

Resection of the presacral nerves was performed June 9, 1933. There was some endometrial tissue at the juncture of the left uterosacral ligament with the uterus. The uterosacral ligament was cut across and all of the endometrial tissue that could be identified was removed. The peritoneum was then closed over, and the uterosacral ligament was adjusted to the uterus. The tubes and ovaries were normal.

In a communication, written Nov. 16, 1933, it was stated that the patient was almost completely relieved of pain, and the periods, which previously had been irregular, were becoming more normal in character.

CASE 14.—A single woman, aged twenty-one years, came to the clinic complaining of intolerable dysmenorrhea which had been present for the last five years. She had begun to menstruate at the age of fifteen years. The periods had been regular and normal for one year, after which menstruation gradually had become painful, until the pain was cramplike, and extended all over the lower part of the abdomen and down to the thighs. In the past year, the pain, which formerly had ceased when the menses had ceased, had continued throughout the intermenstrual period. The cervix had been dilated on three different occasions without much improvement resulting.

The uterus seemed somewhat nodular to bimanual examination. Laparotomy was performed Sept. 15, 1933. There were three adenomyomas, each about 1 cm. in diameter, and one about 5 cm. in diameter, on the posterior wall. Also, there were three small adenomyomas on the anterior wall; all of which were excised. As a further procedure for the relief of the dysmenorrhea, 2 cm. of the presacral nerves were resected.

The patient was entirely free from any pain throughout the menstrual period which occurred during her convalescence in the hospital. A report received November 14 disclosed that she had been completely relieved of the former dysmenorrhea although the menses were somewhat increased in duration and amount.



## COMMENT

Nine patients obtained 100 per cent relief, two 95 per cent relief, and three 75 per cent relief. These figures agree satisfactorily with those reported from foreign countries, and on the basis of this alone, the method should be continued in use until some more simple method is established that will give the same beneficial results.

Two very important questions immediately come up for solution: first, what is the effect on menstruation, and second, what is the effect on parturition? Section of the superior hypogastric plexus does not alter the normal menstrual cycle. On the other hand, menses which have been scanty, or prolonged and excessive in amount, have been altered so that the duration and amount are more within the normal range. This has also been the experience of Fontaine and Herrmann. It is not uncommon, however, to have some postmenstrual bleeding soon after the plexus has been resected if the operation has been performed directly after a menstrual period. Fontaine and Herrmann attribute this to the immediate intense passive congestion of the pelvis, but this does not in any way interfere with the subsequent menstrual period, which occurs at the normal time. Of interest in this connection is the work of Buchheim and Zaleski, who showed that the lutein hormone exercises its action aside from all nervous influences, but that the effect of these hormones can be augmented by increasing the vascularity of the part; such increased vascularity follows sympathectomy.

Pregnancy has not occurred in any of our patients since the pre-sacral resection was performed, although 7 of the patients were married and previously had had children. However, there are many cases on record in which normal parturition took place after patients had been subjected to resection of the superior hypogastric plexus for relief of some painful condition in the pelvis. Furthermore, Gerstmann observed that neither section nor complete destruction of the sacral part of the spinal cord will prevent childbirth, but will only make it necessary to apply forceps when the head reaches the pelvic floor. Also, Rein has reported spontaneous birth of young rabbits following section of all the extrinsic nerves of the uterus.

The percentage of pain that is attributed to pathologic lesions in the pelvis other than to dysfunction of the sympathetic nervous system is difficult to estimate. It is common knowledge, however, that adenomyomas and endometrial implants produce more dysmenorrhea than fibromyomas. In Case 14, the large number of adenomyomas removed proved to be the major factors in the etiology of the patient's dysmenorrhea. Endometrial implants on the under surface of the broad ligaments, the suspensory ligament of the ovary, and especially at the juncture of the sacral ligaments with the uterus, produce an unusually high percentage of painful periods. These two conditions, adenomyomas and endometrial implants, are, I am sure, greater factors in the production

of dysmenorrhea than all of the other so-called associated pathologic lesions except malignancy. Primary dysmenorrhea unassociated with other pathologic lesions is more common than it is supposed to be. Six of our 14 patients had no pathologic condition to account for the dysmenorrhea; yet 5 of them received 100 per cent relief and one 75 per cent relief from section of the presacral nerves only. In 8 cases, other surgical lesions in the pelvis were corrected at the same time, and the same percentage of good results was obtained.

The advisability of resecting the presacral nerves, in addition to correcting other surgical lesions in the pelvis at the same time, seems to have been satisfactorily settled by Cotte.<sup>6</sup> He showed that in more than 200 cases, in which pelvic sympathectomy was combined with other procedures, his results were far superior to those which he obtained in an equally large series of cases in which only the ordinary gynecologic procedures were carried out. However, 6 of the patients in this series, and those reported by Michon and by others, are evidence that in properly selected cases of functional dysmenorrhea, complete and lasting relief follows simple section of the superior hypogastric plexus.

All patients who have various degrees of uterine displacement, or cystic disease of the ovaries, with irregular menses, should be given proper medical and nonoperative gynecologic treatment, which should include the treatment suggested by Novak and Reynolds. If these fail, operative interference should be considered. Palliative operations on the pelvic organs in these cases do not ordinarily give lasting results; therefore, many young women are castrated, or undergo total hysterectomy. Fontaine and Herrmann aptly stated that all of these surgical procedures have been carried out as treatment of a symptom-complex which, originally at least, was only the result of some functional derangement of the pelvic sympathetic nerves. This type of patient is usually completely relieved of the pelvic pain by simple section of the superior hypogastric plexus, without sacrifice of any of the internal genital organs, and without influence on subsequent marriage or on the ability to bear children.

#### SUMMARY AND CONCLUSIONS

The results obtained from resection of the superior hypogastric plexus would indicate that the primary etiologic factor in dysmenorrhea is dysfunction of the pelvic sympathetic nervous system. When this dysfunction is corrected by resection the benefits are permanent, while the functions of normal menstruation and childbirth are not disturbed. If menstruation has been abnormal in amount and duration, there is a marked tendency for menstruation to become normal. Pregnancy has not occurred following sympathectomy in this series of cases, but a sufficient number of cases has been reported to determine that this function is not altered.

The cases of dysmenorrhea are divided into two groups. The first group includes those cases which are unassociated with any other pelvic pathologic condition, while the second group includes the cases in which other pelvic surgical conditions are present which may contribute to the dysmenorrhea.

Resection of the presacral nerves is indicated in both groups, but only after medical and nonoperative measures have failed to give adequate relief. Other coexistent pathologic conditions should be surgically corrected at the same time sympathectomy is performed, since the results are far better. In this series almost complete relief was obtained in all cases.

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#### DISCUSSION

DR. CHARLES A. BEHNEY.—Recently we have employed pelvic sympathectomy for pelvic pain not associated with malignant diseases, in two patients whose chief complaint was dysmenorrhea. In five others there was an element of dysmenorrhea, but the predominant complaint was pelvic pain. Four in this series of 7 cases had either unilateral or bilateral palpable ovarian enlargements. Two of the patients had retrodisplacements of the uterus.

Whenever there was associated pelvic disease, it was corrected at the time of the operation. Two patients had suspensions of the uterus and one had a diseased appendix removed. In two others with apparently normal pelvic structures prophylactic appendectomies were done. Both of the patients who had dysmenorrhea only, were completely relieved. Of the five patients who had pelvic pain with associated dysmenorrhea, only three were relieved of their dysmenorrhea, while all were relieved of pelvic pain.

The evaluation of this operation for the relief of pelvic pain and dysmenorrhea requires a longer period of observation than has been possible in our experience. Leriche has shown that pain sometimes recurs. He has done secondary operations for recurrence apparently due to the imbedding of the proximal nerve fibers in scar tissue.

We have attempted this operation 22 times in patients with pain due to advanced carcinoma. In one patient with a rapidly advancing Stage IV carcinoma of the cervix and a frozen pelvis, the posterior peritoneum was thickened and was plastered down against the prevertebral fascia in a dense sheath. She survived the operation and lived for two months. There was obviously no relief of pain. The case in

which we failed to remove the plexus is included in the series because there will always be patients in whom the operation is technically impossible.

Of these 22 patients, 16 were relieved of pelvic pain for the remainder of their lives. Two of them are still living. One has been alive for over thirteen months and is still free from pain. It must be remembered, however, that 7 of these patients lived for less than four weeks. Had they lived longer some of them might have developed recurrences.

The postmortem findings in these 7 patients revealed: One death due to an undetermined cause, one patient died three weeks after operation from pericarditis, 3 died of uremia, and 2 of peritonitis. In Stage IV carcinoma of the cervix, this operation is evidently accompanied by more than the average danger of peritonitis. Of the six failures, five were either temporarily or partially relieved of pain. One of them was relieved of her abdominal pain, but on the eighth day developed pain in the leg which required just as extensive narcosis as had the abdominal pain of which she originally complained. In three of our patients pain in the legs was relieved by sympathectomy. Such pain may sometimes be due to invasion of the sympathetic fibers which accompany the great vessels to the legs, rather than to involvement of the sciatic nerve to which it is so often ascribed.

The operation that we use is essentially like that so clearly described by Counsellor, except that in operating for pain from carcinoma we do a more extensive resection. We begin our incision about one and a half or two inches above the umbilicus. This enables an exposure of the aorta as high as the origin of the inferior mesenteric artery. We start to resect the plexus just below this point and remove the entire plexus as far into the hollow of the sacrum as possible. Our purpose in doing such an extensive resection is to remove all collateral branches which might transmit impulses of pain.

Resection of the presacral nerve will not relieve pain from obstruction of the ureters, from bone involvement, or from metastases. In two instances troublesome diarrhea caused painful irritation about the anus and temporarily prevented complete relief. One patient had pain in the urethral region which was relieved by irrigations. Another developed an ischiorectal abscess, and she was comfortable only after that had been drained.

We have had four patients who had rectal incontinence for as long as three weeks. It has never been permanent. We had two patients with vesical incontinence, but both recovered within forty-eight hours.

We regard this operation as a valuable procedure in young women. We feel less reluctant to leave cystic ovaries since we have recourse to a procedure which is as promising for relief of pain as is resection of the hypogastric plexus. It should be employed only in those cases of intractable dysmenorrhea in whom formerly, despite the youth of the patient, surgical or irradiation sterilization was practiced. It should always be reserved for patients who have failed to benefit from more conservative treatment.

The operation is not difficult for any one who is familiar with pelvic surgery. It is not especially shocking. The incision is situated so that the recumbent posture does not interfere with healing of the wound. There is no danger of paralysis, either sensory or motor. While one can never promise complete and permanent relief, I feel convinced that more general trial of this operation will prove its usefulness in properly selected cases.

DR. ROBERT T. FRANK.—Regarding the treatment of dysmenorrhea I have experienced over a period of thirty years so many disappointments, treatments, and procedures that I regard every new development with interest, but with a great deal of reserve. I have seen innumerable women with dysmenorrhea, and yet in thirty years I can recall only two cases in which I advised induction of amenorrhea by

x-ray. I have never performed hysterectomy or any other abdominal operation for dysmenorrhea per se. The cause of dysmenorrhea is as unknown today as it was thirty years ago. From the viewpoint of endocrinology it has struck me, and many others, that the "dysmenorrheic patient" regularly falls into a group that is under function constitutionally, pelvically, and psychically. Certain groups of young women are particularly subject to this trouble—those of sedentary occupation, those who are harassed by the stress of life, by overwork. Many of these patients respond to any show of interest, to anything which promises relief. Usually the effect is only transitory. I have seen women who have suffered from primary and secondary dysmenorrhea who certainly disproved any logical basis for the earlier dilating operations by having the dysmenorrhea return or be unrelieved after full-term deliveries.

I feel that the profession at large should be seriously warned against contemplating operative procedure for the average case of dysmenorrhea, that perhaps in the course of many years an active gynecologist may be confronted with one case where the situation is so desperate—the patient has perhaps become a morphinist—where the choice is between a wrecked life and an operation which does not involve too much danger.

DR. VIRGIL S. COUNSELLOR.—In reply to Dr. Holden's question, I would say that in every instance we discuss the nature of the operation with the patient, but unfortunately a good many patients do not grasp what we have talked about when we get through. We do discuss it with them, however, and explain to them what we wish to do in the hope that it will take care of their pain. Their interest is not so much in the operation as it is in the amount of relief to be obtained by it.

In only one of the 14 cases was there associated Raynaud's disease. This may be evidence of a disturbance in the sympathetic nervous system. There was no evidence of any spastic colitis or spasm of the ureter. Two patients had some disturbance of vesical function. There were 2 or 3 ounces of residual urine for the first forty-eight hours and then it gradually subsided. Incontinence of the rectum or of the bladder have not resulted.

A great many of these 14 patients were school-teachers and stenographers. Five patients less than thirty years of age were married and had children.

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**Beaver, Donald C.: Persistent Truncus Arteriosus and Congenital Absence of One Kidney With Other Developmental Defects, Arch. Path. 15: 51, 1933.**

Beaver reports the following postmortem findings in a 3,100 gm. male, full-term infant who died seven days postpartum: The interventricular septum was patent near the base of the heart; there was a common aortic and pulmonary trunk (persistent truncus arteriosus). This structure carried a mixture of arterial blood obtained from both the right and left ventricles. The orifice of this common arterial trunk was guarded by 4 semilunar valves. The ductus arteriosus could not be identified beyond the orifice of the pulmonary artery; the truncus ascended as the aorta. No innominate artery existed on the right; the common carotid and subclavian arteries had independent ostia.

The left kidney and ureter were absent (Agenesis). There were an accessory pancreas and accessory spleen, both identified microscopically. The persistence of the truncus arteriosus in this case was due to a failure of the aortic septum to develop, a true arrest of development.

W. B. SERBIN.



## PREGNANCY IN TUBERCULOSIS\*

GEORGE THOMAS PALMER, M.D., SPRINGFIELD, ILL.

WHEN I was invited to speak before your Society, I was inclined to think that, out of over twenty years of tuberculosis sanatorium experience, I would find much of interest to the gynecologist and obstetrician. As I reviewed our material, however, I was impressed with the fact that, so far as pelvic conditions are concerned, I could offer very little of significance and so I fell back upon that subject which is always of the utmost importance to us and one on which there is occasion for clearer understanding between the physician and the obstetrician: the question of pregnancy in tuberculosis.

With the prolonged stay of patients in the sanatorium, averaging something more than six months, and with the complete control we have over these patients in a secluded environment and especially with the follow-up, which often extends over years, there is an opportunity for leisurely and thorough observation and for the completion of satisfactory records. A review of these records, covering a period of years, discloses a surprisingly large number of ailments entirely independent of the tuberculous condition, with, of course, all of the ordinary complications of the disease as well as many cases of those ailments commonly regarded as more or less intimately associated with tuberculous infection. The great frequency of these borderline conditions and the opportunity for undisturbed and prolonged observation, suggest that the more thorough study of sanatorium patients might throw some light on other fields of medicine.

For example, the frequency of tuberculosis associated with thyroid dysfunction and the numerous instances in which thyroid symptoms, including the high metabolic rate, disappear under routine sanatorium treatment without special medication, raise the question as to the extent to which tuberculosis may be the causal factor in certain thyroid disorders. The occasional cases of progressive tuberculosis, in which the patient, in her earlier stages, has had repeated negative Kahn or Wassermann reactions; but where, in the advanced stages, positive Kahn tests are found, raises the question as to whether advanced tuberculosis may not, in itself, be responsible for the positive Kahn reaction. Dunner and Mayer, of Berlin (*Med. Klin.*, June, 1933), recently raised this question which, for some time, has been in our minds; but without venturing a definite opinion. However, we accept a plus Kahn in advanced tuberculosis with some skepticism as to its

\*Read before the Chicago Gynecological Society, December 15, 1933.

significance. The very great frequency of ischio-rectal abscess and anorectal fistula among our tuberculous patients has raised the question as to how specifically these conditions may be regarded as tuberculous. In our diagnostic service, we have felt that a history of ischio-rectal abscess is to be regarded almost as suggestive of tuberculosis as pleurisy with effusion and, with succeeding years, we have felt little inclination to depart from our rather arbitrary position. However, since most of our patients in the sanatorium are unmistakably tuberculous, our experience cannot be very illuminating. However, we have been reluctant to accept the presence or absence of the tubercle bacillus in the fistulous secretions as final, since we have had several cases of more or less advanced tuberculosis in which the secretions have proved negative on guinea pig inoculation. It may be significant that these patients, at the time the tests were made, had negative sputum.

Our experience with about 2,500 tuberculous patients, the majority of whom are women, offers little of interest to the gynecologist. While we have had the incidence of pelvic disease which one would expect to find in the average group of this size, the number of cases of tuberculous involvement of the pelvic organs, except in terminal cases, has appeared to have been relatively small. Perhaps this is due to the fact that, until the past few years, we have not been particularly "gynecology minded." With the addition to our active staff of an obstetrician, who is also interested in gynecologic work, our future records may prove more interesting.

Incidentally, it will be borne in mind that most of our patients are constantly confined to their beds for months or even years, so it is possible that many of the ordinary gynecologic conditions are less disturbing than if the patients were on their feet and engaged in the ordinary duties of life. In our far advanced and terminal cases, pelvic involvement is doubtless more or less frequent; but, usually, at that time, the location, character or extent of involvement is of little moment, as compared with the extreme gravity of the general tuberculous condition. Autopsies in a small, private sanatorium such as ours are extremely rare and yet, with the great frequency of intestinal tuberculosis with localized or general peritonitis, the involvement of the pelvic adnexa, either through the blood stream, the lymphatics, or by contiguity, must be relatively common.

Out of our rather limited experience, however, we have grown to be quite conservative so far as surgical intervention is concerned. We are inclined to agree with Thomas and Kinsella,<sup>1</sup> that, in tuberculous lesions, surgical treatment is rarely an emergency and that operation should be deferred until the patient is in the best possible condition. The treatment must aim at the patient as a whole and not alone at the local lesion. Delay in operation is frequently beneficial rather than

hurtful. In bilateral, and inoperable renal tuberculosis, it is often astonishing how the patient will improve under routine sanatorium treatment with little more than the usual palliative measures. Our experience has impressed us that the tuberculous patient with gynecologic disorders, will do far better if she may have the benefit of sanatorium care until her general condition is at its best and if she may have sanatorium care after operation.

While our lack of attention may account for the unimportant showing of gynecologic conditions in our records, the question of pregnancy among the tuberculous presents itself with an insistence which will tolerate no indifference. The intimate and friendly relationship established in the sanatorium and the follow-up of several years, if the patient is to attain recovery, afford us an especially definite knowledge of the ultimate outcome with our patients. In the light of prolonged observation with these patients, we are more and more impressed that pregnancy, in any tuberculous woman, is little short of a tragedy, the remedy for which is not satisfactorily supplied by even the most intelligent decision as to whether we shall interrupt or permit the patient to go on to term.

There has been unending conflict of opinion as to the degree of danger of pregnancy in tuberculosis, varying from sweeping and unwarranted pessimism to equally or more unjustifiable optimism. In the face of the overwhelming evidence, we may even yet hear the assertion that pregnancy is harmless if not actually beneficial. This rather commonly accepted popular belief has been responsible for a lamentable sacrifice of human life.

The extreme variance in opinion on the part of obstetricians, general practitioners and those of us who are dealing constantly with tuberculosis, is largely due to the difference in conception in regard to diagnosis. If the diagnostic standards in tuberculosis were more uniform, if all classes of physicians recognized the disease equally early and if all had the same ideas of the seriousness of any form of clinical tuberculosis, we would talk more nearly the same language. Certainly the more one sees of tuberculosis, the more formidable and grave the disease appears.

The observations of Metzger<sup>2</sup> may be accepted as representing a reasonable middle ground in regard to tuberculosis and pregnancy. He holds that, in the true incipient cases, practically without symptoms, pregnancy will light up active disease in 3 per cent of cases. In healed tuberculosis, even of long standing, the outlook is not so good. Quoting the axiom that has been handed down to us, he says that 50 per cent of these patients will stand one pregnancy very well. A second pregnancy is most likely to aggravate the tuberculous condition. A third pregnancy is likely to result in death. In active tuberculosis, with only moderate involvement, 75 per cent are made worse by pregnancy, while in advanced, active cases, 90 per cent die during the puerperium.

Obviously, in the face of these facts, the avoidance of pregnancy is of the utmost importance. Certainly no woman should consider pregnancy for at least two years after the complete arrest of her tuberculosis, and the diagnosis of arrest should not be based upon merely a routine office examination. If there is an urgent desire for children, the arrest of the tuberculous condition should be determined by repeated hospital or sanatorium observations of from a week to a month, in which every available diagnostic means is employed. Incidentally, one of the most valuable of the tests of the condition of the patient and fitness for motherhood is to be found in the blood sedimentation test. In any patient who has had tuberculosis, it is our practice to doubt arrest, regardless of physical signs, temperature, or x-ray findings, if the sedimentation, according to the graphic method of Cutler, remains above 10.

While many tuberculous patients appear to improve throughout pregnancy, there seems to be a decided tendency to the aggravation of mild tuberculosis or the activation of a dormant or previously unrecognized tuberculosis during the first three months. Occasionally the co-existence of pregnancy with newly activated tuberculosis is most confusing. The suppression of menstruation may be attributed to the tuberculous condition. Slight pulmonary hemorrhage may be regarded as vicarious menstruation. It may be two or three months before the physician awakens to the fact that he is dealing with pregnancy complicating a newly developed, active tuberculosis.

But whether we are dealing with pregnancy in a definitely tuberculous person or whether the early pregnancy has activated a previously unrecognized tuberculosis, we are face to face with the troublesome question of what to do about it. We are often inclined to feel that, in those cases which we interrupt, we wish we had permitted the patient to go on to term. In those cases in which we permit pregnancy to continue, we wish that we had aborted. Perhaps the wisest course is to place the patient, regardless of the activity or inactivity of the tuberculous condition, under sanatorium care immediately upon the diagnosis of pregnancy and to defer our decision for a period of three months. If the patient improves during these early months, she will probably go through pregnancy satisfactorily. If the tuberculous condition grows progressively worse during the first three months, the outlook is grave and interruption is probably advisable. Menge points out that abortion is usually unnecessary if sanatorium care is adopted immediately upon the diagnosis of pregnancy. This seems quite reasonable when we bear in mind that pregnancy is usually a serious handicap to the tuberculous mother and when we likewise bear in mind that home care of the tuberculous is rarely successful. In other words, the sanatorium care tends to compensate for the hazard of pregnancy.

The experience in Russia,<sup>3</sup> where almost 12,000 abortions were done for economic reasons, under state supervision, entirely with secrecy, and under the best surgical conditions, indicates that the operation is not without danger even in healthy women. The impaired vitality of the tuberculous may be presumed to increase the operative risk. The very patients who are good operative risks, are those most likely to go through pregnancy and labor without serious consequences.

In cases of active tuberculosis, the general results of abortion are uncertain. In advanced tuberculosis, abortion is frequently followed by serious if not fatal aggravation of the disease. Glaser,<sup>4</sup> of Berlin, probably correctly summarizes current opinion when he says that, in the earlier or quiescent or moderately advanced cases, the course of the disease is not rendered more satisfactory by interruption than by permitting the patient to go to term, provided the patient is given every possible advantage for improvement during the pregnancy. Kehrer, of Dresden, advises close observation without interruption for patients with latent, arrested or early cases, preferably with sanatorium care. For moderately advanced, active cases, he recommends induction of abortion. In the far advanced, active cases, the results of abortion are so unsatisfactory that noninterference is to be preferred except that, in certain cases, induction of premature labor may be carried out to save the child prior to the death of the mother. In all cases, except terminal cases, in which there is complicating laryngeal tuberculosis, the wisdom of interruption is unquestioned.

Sterilization is a subject for endless controversy. In our own practice, we are so impressed with the grave hazard of pregnancy, even in apparently cured tuberculous patients, that we usually advise sterilization in all cases in which we sanction abortion. There may be exceptions with especially intelligent patients with cooperative husbands; but certainly repeated abortion is not to be considered.

With our increasing experience with lung compression and our observation of its favorable effect upon tuberculous involvement, we are inclined more and more to wonder if the very common flare-up of tuberculosis in the puerperium is not partly a result of the physical strain of labor; but chiefly the consequence of sudden evacuation of the uterus with lowering of the diaphragm with reexpansion of the lung. In other words, we are inclined to feel that the improvement noted in the last six months of pregnancy is partly due to the elevation of the diaphragm, such as we obtain in the phrenic operation, with limitation of the respiratory excursion. The rapid reexpansion of the lung, following the emptying of the uterus, is about what we should expect if we should suddenly withdraw the air from the pleural space in a patient with active tuberculosis whose lung had been under compression by artificial pneumothorax.



With this idea in mind, we have recommended artificial pneumothorax or the resection of a portion of the phrenic nerve during the course of pregnancy, our preference being the phrenic operation. In case artificial pneumothorax is employed, we have advocated more frequent and more generous administration of air immediately following labor. From our necessarily limited experience, we are inclined to feel that this procedure is extremely beneficial. Glaser holds that there should never be interruption in a fairly unilateral case until some form of collapse has been undertaken.

The effect of the tuberculous condition of the mother upon the child was formerly as vigorously debated as most of the other phases of this subject. Edgar, writing in 1906, was convinced that the children of tuberculous mothers were usually delicate and undersized with a tendency to active tuberculosis. Williams, writing in 1915, says that these children are usually large and well developed. Edgar felt that these infants had an hereditary predisposition to disease. Whether they have this predisposition or whether, on the contrary, they have an increased immunity is still a matter of controversy. Our own opinion is that the children of tuberculous mothers are no more likely to have tuberculosis than the children of any other group of mothers in more or less impaired health, *provided* they are removed from the mother and from the infected home immediately after birth.

Forsner recently reported that of the children immediately removed from the tuberculous mother, 82 per cent were living and well at the end of three years and that but 6 per cent showed any signs of tuberculosis. Of those cared for by the mother, 52 per cent were living and well in three years and 45 per cent had developed definite tuberculosis.

Briefly, our experience indicates that interruption in dormant, quiescent, or early active cases, should not be carried out until after three months of sanatorium care, with some form of collapse in suitable cases; that all patients with any degree of tuberculosis, either active or quiescent, should be under sanatorium care for the greater part of pregnancy and during the "critical six months" after delivery; that, if possible, some form of collapse should be instituted to anticipate the sudden reexpansion of the lung, incidental to the evacuation of the uterus during labor; that the labor should be made as easy as possible, with relief of pain during the first stage and the shortening of the second stage; that all children should be immediately removed from the tuberculous mother.

#### REFERENCES

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## METHOD OF STUDY AND TREATMENT OF MENSTRUAL DISTURBANCES OF ENDOCRINE ORIGIN

C. A. ELDEN, M.D., ROCHESTER, N. Y.

*(From the Department of Obstetrics and Gynecology, University of  
Rochester School of Medicine and Dentistry)*

THE treatment of menstrual disturbances must be along endocrine lines after anatomic and pathologic pelvic causes are eliminated and systemic diseases ruled out. The advances in the field of endocrinology, particularly of the gonads and their relation to the other ductless glands of the body and to each other, are responsible for the change of treatment from empiricism toward specificity. Menstrual disturbances have been noted in various endocrine and nonendocrine diseases since early times<sup>1</sup> but until recently<sup>2, 3, 4</sup> no attempt has been made to correlate these disturbances with endocrine findings. The etiology of many menstrual disturbances is still unknown and much that is written may have to be forgotten in the future. Sufficient endocrine physiology is known to warrant a systematic study of menstrual disturbances which has for its purpose more exact diagnosis and specific treatment.

The method of study adopted here is in part taken from the procedure of Rowe and Lawrence<sup>5</sup> and in part originated here for our particular needs. All acute infectious, chronic infectious, and blood diseases are ruled out since they very often simulate endocrine disturbances.<sup>5, 6, 7</sup> Pelvic pathology and pregnancy, normal or pathological, must also be eliminated. The patient is therefore admitted to the hospital for complete history, physical and laboratory examination, and necessary operative procedures. If these findings suggest a glandular basis for menstrual disturbance, subsequent history relative to the endocrines is taken, and the patient further examined for related stigmata. Following this, further laboratory procedures are carried out. A basal metabolism test is made followed by a venipuncture for the determination of blood sugar, nonprotein nitrogen, urea, uric acid, and creatinine. These four nitrogen-containing constituents and sugar are the significant substances determined and closely parallel the urinary findings. Significant variations are shown in the high uric acid content of pituitary disease and the adrenal group, but in the latter the blood sugar is low. High residual nitrogen is also characteristic of the adrenal group. These findings are used in the differential diagnosis of endocrine disturbances after nonendocrine disease has been ruled out. Following the venipuncture a galactose tolerance test is done. In addition, in this clinic, the estrin level is determined on a twenty-four-hour sample of fresh urine. It has been shown<sup>8, 9, 10</sup> by using three days' output of urine, that the level of estrin during the menstrual period is low, averaging 10 rabbit units. This level gradually rises to a peak at about the midpoint of the intermenstrual period, averaging 120 rabbit units, when it gradually falls off to the low level again at the next menstrual period. In certain types of amenorrhea and metrorrhagia the estrin content during the cycle is extremely low and variable. Similar studies<sup>11</sup> have been made on the blood and urine but we have not determined blood estrin levels in this clinic. The

determination of the level of urinary estrin gives a measure of ovarian function and indirectly the function of the anterior pituitary gland.

It is necessary in extracting estrin from urine that the urine be fresh and distinctly acid, since it has been shown<sup>12</sup> that the estrin content varies with the age and reaction of urine. Consequently, in all our studies, a day's output of urine, not more than twenty-four hours old, is made distinctly acid with HCl and immediately extracted with benzene in the continuous extractors. We have found that from twelve to sixteen hours is sufficient time to extract all the estrin. The benzene solution of estrin is placed in a beaker and the solvent evaporated. The residue is taken up in a definite amount of oil, usually 12 c.c., and this is injected in accurate graded doses into from four to sixteen castrated female rats. Vaginal smears are taken to determine the smallest amount of the extract required to bring the animals into heat. From this the estrin level for the day is calculated.

Another sample of urine is tested for the presence or absence of sugar, albumin, urobilogen, and the sediment is examined microscopically.<sup>5</sup>

If the history, physical examination, and laboratory procedures seem to indicate disease of the pituitary gland, then accurate visual field, blind spot measurement, and stereoroentgenograms of the skull centering on the pituitary fossa are made. The complete study of the patient takes from about ten days to two weeks. During the course of study, diagnosis or treatment, various laboratory procedures are repeated as seem necessary.

By the above method some sixty patients have been studied for over a period of from six months to two years; some successfully, others not, as indicated. No attempt will be made to classify menstrual disturbances at this time. We have tentatively grouped our cases based on the type of menstrual disturbance and the endocrine gland which seemed primarily responsible. A few representative histories of cases follow.

#### *Primary Amenorrhea and Oligomenorrhea*

CASE 1.—A twenty-year-old nullipara whose menstrual cycle varied from two to six months since onset at fifteen; periods were scanty, requiring only three pads. No other symptoms or signs of endocrine disturbance except male distribution of pubic hair, marked hirsutism of forearms and legs, infantile breasts and genitals, shoulders broader than hips, and male type of larynx. Laboratory findings reveal basal metabolism rate, minus 13 per cent; tolerance for galactose, increased; blood chemistry within normal limits, urinary estrin, 12 rabbit units. Fifteen-grain daily doses of enteric-coated anterior pituitary gland for eight months did not change the menstrual cycle. There was no change in the size of the uterus.

This type of case and those with only infantile genitals (we have studied eight of this type) apparently represent a failure of the endocrine apparatus, probably the pituitary gland, before puberty. The main stigmata in this type of case are infantile genitals and breasts and the hirsutism. Genital hypoplasia<sup>13</sup> is responsible for about 10 per cent of cases of sterility with associated menstrual disorders. Other sterility studies<sup>14</sup> have shown that 54 per cent of the women have genital hypoplasia; 65 per cent have evidence of endocrinopathy still existing; 14 per cent gave a history which suggested early disturbance of endocrine function leaving as a residue various degrees of permanent incomplete development of the reproductive organs. Our experiences with this type of case have been disappointing. We have been unable to initiate a menstrual cycle or increase the size of the genitals by antuitrin-S or from 10 to 25 grains in daily doses of desiccated anterior pituitary gland. If this type of case were seen at, or before, puberty, perhaps the hypo-

plasia could be prevented by proper preparations of the pituitary gland which include the growth-promoting hormone. This opinion is held by others.<sup>14</sup> At this point it should be noted that the injudicious use of preparations made from the urine containing the anterior pituitary-like substances should be discouraged until more is known concerning the action in the human. It has been shown<sup>15</sup> in the monkey that these preparations cause a cessation of ovarian activity with atresia of the large follicles and hyalinization of the small follicles while the anterior lobe or extracts of the anterior lobe cause follicular growth. Reasoning from this, then, some of the successfully treated cases of menstrual disturbances reported, using preparations from urine of pregnancy, were probably attained because of similar pathology in the human resulting perhaps in a temporary sterility with secondary amenorrhea.

#### *Secondary Amenorrhea*

CASE 2.—A twenty-nine-year-old married nullipara complained of amenorrhea of three years' duration following a normal twenty-eight-day cycle beginning at the age of thirteen years. Coincident with the amenorrhea there was a marked iritis, a gain of 40 pounds' weight, loss of libido, depression, and lassitude. All accessible and questionable foci of infection were eliminated. No evidence of tuberculosis or syphilis. The physical examination was noncontributory. Laboratory findings showed a basal metabolism rate of minus 22 per cent, galactose tolerance normal, no estrin in the urine. Patient was given small doses of thyroid which were increased, over a period of months, up to  $7\frac{1}{2}$  grains daily. During this interval of six months, she menstruated three times. On  $7\frac{1}{2}$  grains daily doses of thyroid her basal metabolism rate was minus 9 per cent and there were 30 R.U. of urinary estrin. The cycle on this therapy was normal as to duration, but occasionally a period would be missed. During the treatment she developed an otitis media and boils in the axilla. Menstruation ceased until the infection was cleared up. Since the beginning of treatment she has lost 14 pounds, is less depressed and states that she can read print for the first time.

Clinically it has been observed that the various thyroid states affect the menstrual cycle,<sup>1, 5</sup> and it has been demonstrated that in the experimental animal<sup>16, 17</sup> there is a definite relation between the ovaries and the thyroid. Hypothyroidism with accompanying amenorrhea may be secondary to infection as indicated by the above case. All our cases of secondary amenorrhea due to hypothyroidism have responded readily to thyroid medication when the maintenance dose is reached, and all foci of infection, if present, are removed.

CASE 3.—A twenty-year-old nullipara complaining of amenorrhea of six months' duration following a normal twenty-eight-day cycle. The significant findings are a slightly enlarged thyroid, mild tachycardia, basal metabolism rate of plus 10 per cent, normal galactose test and blood chemistry. Following small doses of Lugol's solution for one month patient menstruated about half the normal amount. Lugol's solution continued for one month more and the cycle has been reported normal for the past six months.

We have had one case of secondary amenorrhea due to mild hyperthyroidism. This case again demonstrates a possible thyroovarian relation. Whether or not the pituitary gland influences this relationship is not definitely established, but evidence<sup>16</sup> seems to indicate that its gonad-stimulating power is increased in the hyperthyroid experimental animal.

CASE 4.—A twenty-three-year-old married multipara who complained of oligomenorrhea and amenorrhea of three years' duration following a normal cycle. The significant findings are a steady increase in weight with girdle type distribution, a

familial history of girdle type of obesity, dry rough skin, basal metabolism rate of minus 8 per cent, increased tolerance for galactose, 20 rabbit units of urinary estrin, hyperplastic endometrium, positive urobilinogen in urine, and increased blood creatinine. Patient was given a restricted diet, small doses of thyroid, and large doses of pituitary medication. For the next six out of eight months, patient menstruated more or less normally and lost 15 pounds in weight.

There have been several cases of secondary amenorrhea due to hypopituitary function. The response of this type of case to enteric-coated capsules of desiccated anterior lobe of the pituitary gland given in massive daily doses has been encouraging but not striking; one of the more successfully treated cases having been reported above. Perhaps larger doses of the gland or a specific hormone containing preparation would be of value in this type of case.

#### *Menorrhagia and Metrorrhagia*

CASE 5.—A twenty-nine-year-old nullipara complained of intermenstrual bleeding of one year's duration, following a perfectly normal cycle. The history, physical examination, laboratory findings, and complete blood studies are normal. Patient was given 100 rabbit units antuitrin-S daily for three days just before the midpoint of the intermenstrual period which prevented this type of bleeding. Because of skin sensitivity patient was given 15 grains of enteric-coated anterior pituitary gland daily for three days just before the midpoint of the next expected period. Similar medication has prevented intermenstrual bleeding for seven months.

Six cases of this type of intermenstrual bleeding have been successfully treated. The bleeding may be of any extent from spotting to an apparently normal period. The bleeding may be physiologic.<sup>18</sup> Most of such cases show nothing abnormal in the endocrine studies so that attention is directed to the theory of menstruation.<sup>19</sup> Presumably the anterior pituitary gland does not secrete one of its hormones at the time of ovulation, and as a result no corpora lutea are formed, and the patient menstruates from a resting type or hyperplastic endometrium. If lutein tissue could be formed at this time either by rupture of the follicle or by supplying the patient with progestin,<sup>20</sup> intermenstrual bleeding should be prevented. The progestational type of endometrium has been produced in the human female<sup>21, 22</sup> with progestin-containing preparations. Since progestin is not available, we have given these patients massive doses, up to a total of 75 grains, in from three- to five-day periods, of enteric-coated anterior pituitary desiccated, at the midpoint of the intermenstrual period. Some patients required this medication for two or three months, others longer. The same effect has been obtained in some cases by using antuitrin-S.

CASE 6.—A thirty-two-year-old para iv who complained of menorrhagia following the birth of her last child two years ago. The periods were markedly profuse, lasting up to ten days and are accompanied by the passing of many clots. Radium treatment elsewhere caused a suppression of the menstrual cycle for three months following which there was a return of the menorrhagia. Dilatation and curettage performed elsewhere showed hyperplastic endometrium. The general history and physical examination are negative. There is a mild anemia, a normal basal metabolism rate, a decreased tolerance for galactose and a urinary content of 125 rabbit units of estrin. A total hysterectomy was done elsewhere, and the gross and microscopic examination showed normal female pelvic organs.

This case represents bleeding due to a hyperfunctioning pituitary gland. Since the pelvic organs were found to be normal at operation it is felt that x-ray therapy to the pituitary gland would have obviated a laparotomy. Favorable results have been reported with this type of medication.<sup>23</sup>



CASE 7.—A thirteen-year-old nullipara who complained of prolonged, profuse menstrual periods since onset at the age of twelve years. The periods have increased until they lasted about fourteen days and were accompanied by the passage of many clots. The past history and physical examination are negative. The laboratory findings showed marked anemia; hemoglobin, 55 per cent; R.B.C., 2,100,000; normal blood chemistry studies; basal metabolism rate of minus 22 per cent; increased tolerance for galactose and 22 R.U. of estrin in the urine. She was given 100 R.U. of antruitin-S daily for five days when bleeding ceased. Twenty-three days following discharge from hospital the bleeding returned as before. She was given anterior lobe medication without effect. The patient was rehospitalized and given ten grains of thyroid. No symptoms developed within five days. She was then placed on five-grain daily doses of thyroid and treated for her anemia. Bleeding stopped in ten days. She has been kept on maintenance doses of thyroid and has had four perfectly normal menstrual periods.

This interesting group of cases of metrorrhagia and menorrhagia at puberty offer many possibilities from an endocrine viewpoint. The first impression of the above case was that the pituitary gland was primarily involved, but, as noted, she did not respond to the second course of pituitary medication and has subsequently had normal menstrual cycles on thyroid medication. It is possible that the rapid growth at the time of puberty in this case caused a depletion of the pituitary hormones and that the thyroid was secondarily involved or that the same picture could be explained on the basis of the thyroid gland.

Many of the cases of metrorrhagia and menorrhagia studied have been difficult to diagnose and treatment has consequently been unsatisfactory. Some of these cases may perhaps be explained on constitutional tendencies. A subsequent history on one of our cases not reported, which was refractory to all treatment, revealed a familial history of both mother and sisters having metrorrhagia and menorrhagia of similar nature which after marriage and pregnancy were spontaneously corrected.

#### DISCUSSION

From the cases herein reported and those that have been studied but not reported, it is obvious that there is no relation between the type of menstrual disturbance and the endocrine gland primarily involved. Very often an impression from the history as to the gland primarily involved is wrong, as is borne out when the case is completely studied. Diagnosis of menstrual disturbances should not be made on laboratory findings alone. One needs only to consider that a low basal metabolism rate may be due to either thyroid or pituitary. A low blood sugar content may be due to the adrenal glands or the pancreas. Hypothyroidism and hyposuprarenalism are at times similar.<sup>24</sup> It is, therefore, necessary to get all the clinical, physical, and laboratory data together in order to establish a diagnosis. Subsequent course of the patient on specific therapy is the criterion of correct diagnosis.

The therapy for menstrual disturbances has varied in different clinics. The use of theelin or similar preparations in the treatment of amenorrhea has received thorough investigation. Most investigators<sup>4, 25, 26, 27, 28</sup> believe that its effect is nil or at best limited, although some have reported favorable results. Perhaps in some of the successfully reported cases of the above authors, the patients menstruated from a resting type or

hyperplastic endometrium. This has been shown in studying the effect of theelin on castrated women.<sup>29</sup> The experimental work on endometrial hyperplasia<sup>30</sup> demonstrates that this condition is the result of the action of estrin. Bleeding may result from all stages of the estrin type of endometrium. It should be remembered, as demonstrated in the animal<sup>31</sup> and recently referred to clinically<sup>32</sup> in the treatment of menstrual disturbances, that the injection of theelin may bring about an inhibition of the pituitary function with decrease in size and physiologic activity of the ovary. It is rather generally agreed that theelin is useful in the treatment of menopausal symptoms. We have used it in this clinic in some few instances as an adjunct of the specific therapy, particularly in those cases where no estrin was demonstrable in the urine. We have been unable to initiate bleeding in a few of our cases of amenorrhea, not reported, by means of apparently adequate doses of theelin.

Anterior pituitary-like preparations prepared from the urine of pregnancy have been given thorough clinical trial and have been used primarily for the treatment of functional uterine bleeding. Favorable results have been reported by many investigators.<sup>4, 28, 33, 34</sup> In view of Engle's recent work<sup>15</sup> on the monkey, the use, as pointed out above, of this type of preparation should be limited. We have used enteric-coated capsules of anterior pituitary gland in massive doses with encouraging results. Lawrence<sup>14</sup> reports that he is able to get a high percentage of normalization of the menstrual cycle with pituitary gland fed by mouth, but he has noted no effect on skeletal growth. Until a gonad-stimulating preparation can be prepared from the gland itself, the use of pituitary-like preparations from urine should be limited.

The use of thyroid extract and Lugol's solution for thyroid diseases is obvious. X-ray therapy to the gland primarily involved is of definite value. Drips and Ford<sup>23</sup> have treated certain types of menstrual disturbances with low voltage over the ovaries and hypophysis and in intractable cases have procured a high percentage of favorable results. They are attempting to standardize the dose by means of animal experimentation, which to the mind of the author is highly desirable for the proper treatment of menstrual disturbances. We have used x-ray therapy in some of our cases with favorable results; we irradiate only that gland which seems to be primarily involved.

Insulin has been used successfully in the treatment of menstrual disturbances.<sup>35</sup> Its use is not without basis since an occasional correction of amenorrhea has been noted in the treatment of diabetes mellitus with insulin.<sup>36</sup> One of the first cases of severe juvenile diabetes mellitus,<sup>37</sup> necessitating 100 units of insulin a day for ten years, improved markedly with the onset of menstruation at the age of nineteen years, so that the insulin dosage was decreased to 50 units a day.

Cortin may be used in cases of adrenal insufficiency in women with secondary amenorrhea. Menstruation has returned with treatment by

cortin.<sup>38</sup> In normal women it has been possible to shorten the interval between periods from three to five days with cortin. This hormone then may be of value in the treatment of menstrual disturbances where the adrenals are primarily involved.

In order that menstrual disturbances be correctly treated, the whole endocrine system should be investigated before treatment is instituted. Hamblen,<sup>4</sup> Rowe,<sup>3</sup> and recently Anspach and Hoffman<sup>2</sup> have studied menstruation with this end in view, and it is by this method of attack that the ultimate solution will be found.

#### CONCLUSIONS

1. It has been demonstrated that any one of the endocrine glands in addition to the ovaries may be responsible for menstrual disturbances. When all disease simulating endocrine disturbance is ruled out, it is necessary to arrive at a diagnosis of the endocrine gland primarily involved by special clinical and laboratory procedure. Treatment is directed at the gland involved and varies according to the nature of the disturbance.

2. Sixty cases studied so far by this method indicate that menstrual disturbances may be due to hypofunction or hyperfunction of the thyroid or pituitary, or to certain types of intermenstrual bleeding at the time when ovulation is supposed to occur, where presumably the anterior pituitary gland fails to cause the rupture of the follicle with subsequent lutein tissue formation. Early menopause must be added to the group of menstrual disturbances.

3. Treatment of amenorrhea due to hypothyroidism and metrorrhagia of the midinterval type has been gratifying. Hypopituitary cases of certain types have responded tolerably well to treatment, and others have been refractory.

4. The results of this method of study are encouraging enough to warrant continuance.

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## THE CHOICE OF METHODS FOR PREGNANCY DIAGNOSIS\*

LEITA DAVY, PH.D., AND ROBERT A. NASON, M.D., MADISON, WIS.

(From the Department of Medicine, Wisconsin General Hospital)

MANY modifications of the original methods for the demonstration of the Aschheim-Zondek principle<sup>1, 2</sup> have been developed in its transition from a biologic problem to a practical clinical test for the diagnosis of early pregnancy. In the attempt to adapt it to the requirements of a routine laboratory, immature rats, both male and female, have been used. Rapidity and simplicity have been achieved by the application of the Friedman and Lapham<sup>3</sup> rabbit ovulation test and of the Schneider<sup>4</sup> immature female rabbit test. Among those who have used the rabbit and the rat or mouse tests in parallel, there is but little agreement as to the comparative accuracy and sensitivity.

All of these procedures, in common with other methods involving biologic endpoints, are subject to a variety of errors. These errors may be due to individual and species variations in the test animals. They may represent faulty technic of such nature as to necessitate special adaptations to problem cases as indicated by the case history or by unusual findings in the injected animals. They may be inherent in the actual limitations of the test. Reduction of such technical errors is largely a laboratory problem which can be solved only through vigilance and experience with a great many cases.

In this laboratory the proportion of problem cases in the first 100 tests run was very low. Recently, through the Wisconsin General Hospital, pregnancy diagnosis was offered, as a routine laboratory service, to physicians throughout the state. With the resulting rise in the total number of tests, there has been a relatively greater increase in the number of specimens from cases of abnormal pregnancy and from cases of endocrinopathy simulating early pregnancy. In an attempt to meet the exigencies of such a differential diagnostic service, the laboratory régime

\*Submitted for publication, November 1, 1933.

has passed through several stages. It has been necessary to investigate such matters as the preservation of specimens to be mailed to the laboratory, the injection technic best adapted to the urine received, the establishment of standards on which to base the final report, management of the animal colonies, standardization of the test animals, and other methods of technical improvement and simplification.

The laboratory organization as it is now in operation is based on experience with tests in more than 800 cases, specimens from all of which have been tested by the modification of the Friedman method which will be described. In several instances the test specimens have also been injected into immature rabbits and the same operative technic used as that outlined for the mature rabbit test. Many tests by the rabbit ovulation method have been checked by parallel tests using a female rat modification of the Aschheim-Zondek procedure. The details of this immature female rat modification will be given in this paper. More than 400 tests have been checked by the subsequent clinical course of the case. Those tests found in error have been carefully analyzed and classified. Correlation of the laboratory observations with the clinical data has led to modifications and precautions which tend to reduce the incidence of errors. It is the purpose of this communication to present such technical details as have contributed to accuracy, expediency, and general laboratory economy in the management of this pregnancy diagnosis service. The incidence of errors and their associated clinical conditions will be considered only so far as they have influenced technical developments.

#### TECHNICAL PROCEDURES

*Management of Urine.*—A. Preservation: Since many of the mailed specimens may be several days in reaching the laboratory, their adequate preservation is a point of considerable importance. It has been found that, although the hormonal activity may not be altered upon standing, an ammoniacal decomposed urine is invariably toxic to both rabbits and immature rats. Boric acid has proved a most satisfactory preservative which also serves to maintain the desired slightly acid reaction. It is not detrimental to the gonadotropic substance and is less toxic than many other recommended preservatives. Ten grams of boric acid adequately preserve and acidify an 8-ounce specimen. Formalin appears to be definitely inimical to the active principle of pregnancy urine. One incorrect negative of this series can be directly traced to the use of formalin in the urine. The injection of the formalin-preserved specimen produced no detectable effect on the ovaries of either immature rats or those of a mature rabbit. A second specimen, obtained two weeks later and preserved with boric acid, gave a markedly positive reaction. One drop of formalin per ounce of urine was added to the remainder of this second specimen and the preparation was kept in the laboratory overnight before injection. This formalinized urine produced no effect in the mature rabbit or in the immature rat ovaries. This seems to be fairly conclusive evidence that the hormone is readily destroyed by formalin.



**B. Toxic Urines:** Specimens have been received which, although definitely acid in reaction, were highly toxic to rabbits. No appreciable reduction in toxicity was effected either by the ether washing method or by the ether-glucose detoxification method of Zondek.<sup>5, 6</sup> Wiesner's sulphosalicylic acid precipitation process<sup>7</sup> was equally ineffective in rendering these urines innocuous to injected rabbits. Extracts prepared by the Lloyd reagent-pyridine elution method developed in this laboratory<sup>8</sup> have given correct results with no toxic effects in the injected rabbits. After three washings with an equal quantity of ethyl ether, these urines are usually sufficiently detoxified for injection into immature rats. All trace of the ether must be driven off before injection. Immature rats are extremely sensitive to injection of small amounts of ether.

**C. Injection Technic:** Both the quantity and number of injections of the test urines have been found to be significant factors in the accuracy and uniformity of result obtained by the rabbit methods. In the extension of the clinical use of the Friedman test, the chief deviations from the technic described by the originators have been with respect to these two points. Friedman and Lapham<sup>3</sup> injected a total of 24 c.c. of urine, in six equal doses over a period of forty-eight hours. Since that time single injection technic, with quantities of urine ranging from 5 to 15 c.c., has been employed by many investigators.<sup>9, 10, 11, 12, 13</sup> Other workers have reported that a higher degree of accuracy is obtained with larger amounts of urine, from 20 c.c. to 30 c.c., administered in two or three injections.<sup>14, 15</sup> Those who advocate a single small injection usually specify that the first morning specimen is required. Obviously the minimum effective dose of pregnancy urine must vary with different specimens. The potency would depend on the hormonal concentration as determined both by the actual concentration of the urine and by the duration of pregnancy.

Since many of the urines received for test at this laboratory are mailed from a distance, it is not feasible to obtain the first morning specimen in all cases. A sample from any ordinary voiding is accepted. To guard against inadequate hormone concentration, a larger amount of the test urine must be injected than would be necessary were the more concentrated first morning specimen available. A study of the relative potency of the day and night urine from several cases of early pregnancy at this hospital has been made. Twenty-four-hour urine collections were obtained. The first morning specimen, or the night voidings, were kept in a container separate from the day voidings. It was found that, on a normal fluid intake of 2,000 c.c. or less, the first morning specimens were approximately twice as effective as the day urines. If the fluid intake were excessive, 4,000 c.c., the day and night specimens were practically the same as to volume, specific gravity, and hormone concentration. In one case of very early pregnancy, no missed menstrual period, a single 15-c.c. injection of the first morning specimen invoked a weakly positive reaction. Twenty-five cubic centimeters of the day urine injected in two equal doses produced large hemorrhagic follicles but no rupture points. Upon the injection of 30 c.c. of this specimen, in two 15 c.c. amounts with a ten-hour interval between the first and the second injection, a markedly positive reaction was observed in the ovaries of the mature rabbit. In several other cases of early pregnancy, dual injection has given a positive result when a single injection of the same total amount of urine either produced no effect or only hemorrhagic follicles. (This is in accord with Friedman's observation<sup>16</sup> that frequent small injections of urine cause greater stimulation to ovulation in the rabbit than a single injection of equal amount. Friedman<sup>17</sup> has also stated that there is less individual variation in the response of rabbits to a given dose of pregnancy urine when multiple injection technic is used than with single injection of the same amount of

urine. The experience of this laboratory leads to agreement with this statement. Although our rabbits are of standard breed, always obtained from the same breeder, and are housed in individual cages at all times, they do not react with any semblance of uniformity to single injections, whether the interval between injection and ovary observation be sixteen hours, as advised by Wilson and Corner,<sup>11</sup> or forty-eight hours, as recently advocated by Reinhart.<sup>12</sup> Urines from cases of known pregnancy have occasionally failed to elicit an ovarian response when injected as a single dose, while the same amount of the specimen administered in two equal doses with an interval of ten or twelve hours between injections has invariably induced ovulation.

As a result of these observations we have now adopted the following routine for the injection of mature rabbits: The test urines, filtered and preserved with boric acid, are taken from the refrigerator and allowed to reach room temperature before injection. With no aseptic precautions, two 15 c.c. injections, with a ten- to twelve-hour interval between injections, are administered by way of the marginal ear vein. Each injection is followed by 1 c.c. of sterile saline injected through the same needle. The saline injection serves to cleanse irritating urinary substances from the vessel wall and thus prevents the fibrosis and occlusion which may result after a few injections if the vein is not washed out. Another precaution against venous occlusion is the use of a small hypodermic needle,  $\frac{3}{8}$  inch length and 26 gauge, for injecting the urine. A small needle also insures against too rapid injection. Rarely is a rabbit unable to tolerate two injections of 15 c.c. each, if given slowly. With slow injection it does not appear necessary that the urine be warmer than ordinary room temperature.

The same general procedure has been applied to the injection of immature rabbits for tests. We have found the subadult animals less uniformly responsive to urines of low hormone content in very early or abnormal pregnancies than are the mature animals. Division of the total injection into two or three doses appears to increase the sensitivity of the immature ovaries to small amounts of the active principle. It seems not improbable that the ovaries of many of these young animals may require one or two stimulating doses before they are in condition to produce corpora hemorrhagica. Since rabbits eighteen weeks' old usually weigh from 1,500 to 1,800 gm., a total injection of 15 c.c. or 20 c.c. corresponds very well with the 30 c.c. injection used in the older rabbits whose weight is usually from 2,500 to 3,000 gm.

In a series of titration experiments in which female, twenty-four-day-old rats were used to determine the minimal effective dose of pregnancy urine,<sup>8</sup> it was noted that in all cases the maximum ovarian response resulted from the injection of 3 c.c. to 5 c.c. per animal. The Aschheim-Zondek method of injecting graded doses of the test specimen seems to be of no advantage in routine pregnancy diagnosis by means of immature female rats. Division of the total amount of urine into five equal doses, given once in twenty-four hours, proved quite as effective as the injection of the same quantity in ten injections at twelve-hour intervals. Extraction of the follicular hormone is not essential to the accurate diagnosis of pregnancy. However, if theelin-free urines are injected into immature animals, the results of a negative test may serve as an index to hyperhypophyseal function in the nonpregnant. Any uterine or vaginal reaction may then be interpreted as due to follicular development, induced by an excess of follicle-stimulating substance in the injected urine. In this laboratory all specimens to be tested by the immature female rat method are washed three times with ethyl ether, poured into evaporating dishes, and placed in a warm chamber (38° C.) for one hour or more to permit evaporation of traces of the ether before injection. Each test animal is given, by subcutaneous injection, 1 c.c. of the ether-washed urine once a day for five successive days.

*Pregnancy Diagnosis by Rabbit Tests.*—A. Selection and Maintenance of Animals: All of our rabbits are obtained from a breeder whose records of age, weight, number of pregnancies, and period of isolation have been found dependable. The young female rabbits are separated from the males at weaning and are kept with other females of the same age until they are eighteen or twenty weeks old. From such a group, animals weighing not less than 1,500 gm. are selected, at seventeen or eighteen weeks of age, for use in tests by the immature rabbit method. For tests with mature rabbits, only such animals are accepted as are known to be six months or more of age, to have had at least one litter, and to have been kept in individual cages three weeks or longer. It is practically impossible to obtain immediately postpartum rabbits from any breeder. However, knowledge of the breeding record tends to rule out individual variations. Fewer refractory animals are encountered, hence greater confidence can be placed in the accuracy of negative results.

Different breeds of rabbits exhibit marked variation as to follicular development. Among the rabbits which we have used, it has been noted that the Australian reds, Australian whites, Flemish whites, and mixed breeds less constantly present ovaries with large follicles than do the standard chinchilla grey rabbits kept under the same environmental conditions.

The environment of the rabbit exerts considerable influence on follicular development. Although kept in separate cages, rabbits brought to the laboratory from ordinary outdoor hutches are not in heat when received. They must be kept in warm quarters for several days before they are physiologically in condition to react to the injection of pregnancy urine. Rubaschkin<sup>18</sup> and others have reported that guinea pigs in captivity breed less frequently in winter than in summer though they may become pregnant at any time if kept warm. This nonbreeding of guinea pigs submitted to low temperature may well be assumed to be due to a lack of follicular development. It seems logical to infer that housing in cold quarters may likewise be responsible for the absence of follicles in the ovaries of rabbits so kept. Stockard and Papanicolaou<sup>19</sup> observed that domesticated animals, particularly rabbits, kept under uniform conditions of temperature and feeding frequently lose the seasonal variations of sexual behavior characteristic of such animals in their native wild. This, no doubt, explains the fact that rabbits kept in isolation in a warm laboratory are, as a rule, constantly in condition to react positively to the injection of pregnancy urine.

Infection in an animal precludes its use in successive tests. Immature and young adult rabbits seldom survive more than one operation if they have coccidiosis. Anesthetization is usually fatal to animals with respiratory infections. Incorrect negatives may result from the use of rabbits bearing staphylococcal infection. In our laboratory, ovaries of animals with stitch abscesses and those of rabbits with suppurating eye ulcers have been found to possess no large follicles. No reaction could be induced in these ovaries by the injection of known positive urines. When the lesions were completely healed, the ovaries were again responsive to gonad-stimulating substance. Animals in which the ovaries have become adherent, encapsulated with scar tissue, or have the blood supply interfered with are discarded from the test colony.

B. Repeated Use of Test Rabbits: Examination of rabbit ovaries by operation has many advantages over that by autopsy. The ultimate cost of the test is lowered by the reduction in turnover in the colony. By repetition of tests in a single animal, standardization of the colony is automatically effected. The first positive result obtained in a rabbit brands that animal as one capable of responding to gonadotropic

material. Reference to carefully recorded descriptions of the appearance of the ovaries of an animal at a previous test is frequently helpful in the interpretation of results which might otherwise be doubtful.

It has been observed that two weeks after the injection of pregnancy urine, the ovaries of immature rabbits have assumed the appearance of those of normal uninjected control animals of the same age. The period of pseudopregnancy in the mature rabbit is of longer duration. The corpora lutea, resulting from stimulation by pregnancy urine, persist for three weeks or longer. Some of the ovaries of these mature animals are so extremely hypertrophied that it is doubtful if they ever resume normal size and appearance. This arouses the suspicion that repeated stimulation of the ovaries to such excessive development may eventually produce a refractory state akin to that described by Hisaw and associates.<sup>20</sup> As a precaution against incorrect negatives, all such results obtained in rabbits that have been used for more than three tests are checked by immediately injecting a test dose of pregnancy urine extract of known gonadotropic potency. A positive reaction, twenty-four hours after the injection, demonstrates the sensitivity of the rabbit and establishes the accuracy of the negative test with respect to that specimen.

Pregnancy diagnosis was still in the status of an experimental procedure in this laboratory when it became apparent that operative technic involving approach to the ovaries by way of midline ventral incision would not permit more than two or three successive tests per rabbit. In spite of extreme care as to asepsis and surgical manipulation, the animal's usefulness was soon terminated by extensive peritoneal infections, herniation with fatal strangulation, intestinal and ovarian adhesions, or bad healing of the external wound. An operative procedure was, therefore, devised for demonstrating the ovaries by way of a dorsal approach. Application of this method has proved highly successful. The difficulties attendant on the transabdominal operation are largely avoided. Many of the animals have been used eight or nine times and to date 5 rabbits have survived twelve tests. Relatively little time is required for the operation; not more than from seven to ten minutes for observation of one ovary or from fifteen to twenty minutes if both ovaries must be exposed. Experience with 800 tests has shown that routine pregnancy diagnosis can be handled without highly trained technicians and with but little equipment or outlay of sterile supplies. The cost of the test is not prohibitive.

The lumbodorsal approach to the ovaries, as developed in this laboratory, had been applied in more than 300 tests when a similar technic was described by Goodale and Flanagan.<sup>21</sup> The two procedures are fundamentally the same although they differ in certain details. The latter may perhaps account for the fact that the test animals of the Goodale and Flanagan colony can be used for no more than three tests, while those of our colony are seldom used less than eight or nine times. With observance of the injection technic described above, no rabbits have been discarded because of occlusion of the ear veins. Neither have we encountered granulation tissue with involvement of the uterine horns or ovaries in the wound. A detailed outline of the lumbodorsal technic as used in this laboratory may be of value.

Female rabbits of the standard chinchilla breed are kept in a warm laboratory for one week before use in the tests. The mature does are known to have been kept in separate cages at least three weeks before delivery by the dealer. Individual cages are also provided for them in the laboratory. It is not essential that the immature rabbits be isolated from other females. The test animals are injected as described in a previous section of this article. Twenty-four to thirty hours after the first injection of test urine, the results are read in the ovaries exposed for observation by the following procedure.

C. *Technic of the Lumbodorsal Approach:* Ether or sodium amytal anesthesia are equally successful. The latter is preferred when there is no assistant to serve as anesthetist. Best results are obtained with the use of 60 mg. of sodium amytal per kilogram of body weight, made up freshly in distilled water and injected intravenously one-half to three-quarters of an hour before the incision is made.\* This time is used to advantage in preparing the animal and in arranging instruments and equipment in readiness for use during the surgical procedure. The instruments may be sterilized by boiling or by placing them in a container with a quantity of 2 per cent phenol sufficient to cover them, rinsing in 70 per cent alcohol and sterile water just before use.

When the rabbit has become fairly drowsy, it is stretched, ventral surface down, upon an appropriate operating table. The lumbar region of the animal is elevated by means of the lumbodorsal support (Fig. 1). The hair is closely shaven or chemically removed from a fairly large rectangular area which extends laterally over

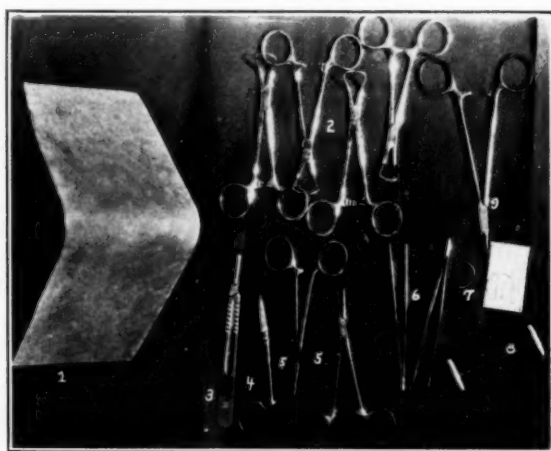


Fig. 1.—Equipment and instruments. 1, Lumbodorsal support (galvanized iron strip, 12 cm. x 26 cm., angle of 110°, rounded rather than sharply bent). 2, Backhaus towel forceps, Rochester pattern (an aid but not essential). 3, Bard-Parker operating knife—No. 4 handle with No. 21 blade. 4, Mayo Dissecting Scissors, curved, 5½ inch. 5, Crile hemostatic forceps, straight, 5½ inch. 6, Tissue or dressing forceps, 6 inch. 7, Suture needles, ¾ circle, No. 16. 8, Surgical silk, black, twisted, No. 9. 9, Needle holder.

the full width of the body and anteriorly from the intercrest line† (Fig. 2) for a distance of 10 or 12 cm. Through the thin skin, the lateral edges of the longissimi dorsi are plainly discerned. If the animal is so stretched that all the vertebrae are in a practically straight line, the ovaries usually lie approximately 6 cm. cephalad the intercrest line and slightly less than 2 cm. laterad the longissimi border. Upon ascertaining the probable location of the ovaries, the site of the prospective incisions may be marked out with mercurchrome or tincture of metaphen. The entire depilated area is cleansed with a liberal application of 70 per cent alcohol.

\*We are indebted to Mr. Frank Maresh of the Department of Physiology of the Medical School for kindly communicating to us the results of his careful investigations as to the dose of amytal best tolerated by rabbits as well as the optimum time required for effective anesthetization of the animals.

†The term "intercrest line" is here used as defined by Schultz (Anat. Rec. 52: 106, 1932) as "the line passing through the right and left iliac crests at the juncture of each lateral ridge with that of the crest."



A working area of 4 to 6 sq. cm., with the site for one of the incisions at its center, is draped with large sterile flats held in place by towel forceps. Stretching the skin taut between the thumb and finger, a straight incision 2 cm. in length is made with the Bard-Parker knife. With a very sharp knife a single quick, firm stroke should incise the skin and superficial fascia down to the fibers of the external oblique abdominal muscle layer. The tips of the curved dissecting scissors are forced between the bands of both the external and the internal oblique muscle layers. By spreading the blades of the scissors, the muscle fibers are stripped apart the full length of the skin incision. The margins of the skin and of the muscle layers are grasped in the hemostats, the weight of which, falling on either side of the body, serves to spread the opening for exposure of the peritoneum. The latter is cut with the curved dissecting scissors. The ovarian and uterine fat now lies exposed and may be easily pushed aside with the tissue forceps disclosing the ovary. The ovarian fat and the ovary are drawn through the incision. The ovary is held in view by firmly pinching the fat at its base in the tissue forceps. After observing all surfaces of the ovary, it is tucked back into its former position and

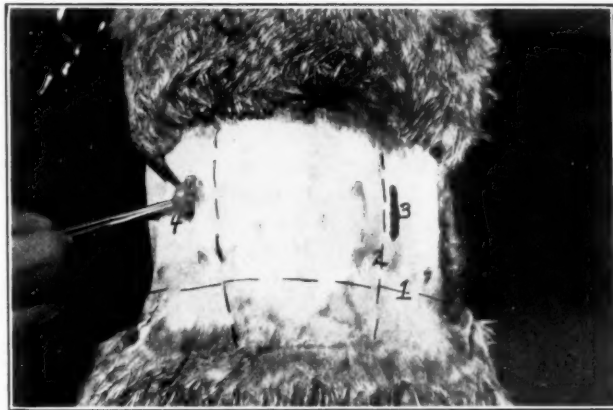


Fig. 2.—Operating field and exposure of ovary. 1, Intercrest line. 2, Lateral border of longissimus dorsi. 3, Probable site of ovary. 4, Ovary exposed for examination.

covered with a fat pad. The wound is closed in two layers. The peritoneum is caught up with the muscle layers, which are drawn together with one or two sutures of black silk. The skin and fascia are similarly sutured. The wound is then dressed with tincture of metaphen and is coated with flexible surgical collodion.

If the first ovary bears one or more ovulation points, the reaction is considered positive and the other ovary need not be observed. The mature rabbits are returned to individual cages after the operation and are not used again for tests until three weeks have elapsed. In the immature rabbit the wounds heal more quickly, and the effects of ovary stimulation disappear sooner; hence it is our practice to use the seventeen- or eighteen-week-old rabbits for three successive tests with an interval of but fourteen days between tests. After the third test the animal is placed in an individual cage, is given four to six weeks of rest, and is then used as a mature rabbit.

D. Criteria for Judgment of Results: The majority of the positive reactions are easily diagnosed. A few findings among both the positives and the negatives are decidedly puzzling and require careful consideration or repetition of the test before a final report can be given with confidence. It is occasionally necessary to

withhold judgment until a second specimen can be obtained for test. Tests in which large clear follicles are the only finding in the ovaries of injected mature rabbits are reported as definitely negative. The absence of large follicles in the ovaries of a mature rabbit is accepted as evidence that the animal was not in heat at the time of the injection and, therefore, not physiologically in condition to react positively to pregnancy urine. The test is then repeated in another mature rabbit. Failure to induce ovulation in the mature rabbit does not necessarily prove the patient nonpregnant but it does prove that, in the particular specimen injected, the concentration of active principle was insufficient to cause rupture of the follicles and liberation of the ova. A negative test on a second specimen, after an interval of two or three weeks, is usually to be depended upon as eliminating pregnancy.

In this laboratory it has been frequently noted that the injection of urines from cases of endocrinopathy in the nonpregnant may produce corpora hemorrhagica and hemorrhagic follicles in the ovaries of mature test rabbits. Many indeterminate results, in which there is evidence of marked stimulation but no ovulation in the ovaries of the mature rabbits, are clarified upon retesting the urine by the immature rabbit or the immature female rat tests. A markedly positive reaction by either or both of these methods insures the accuracy of a positive report, while failure to obtain a definite response confirms the result as truly negative for pregnancy.

In this series there are 236 pregnancies reported as having terminated in normal deliveries. Among them there was but one urine which failed to cause ovulation in the ovaries of the mature rabbit used for test. In two abnormal pregnancies, which terminated in abortion, ovulation points were not observed, although there was marked ovarian stimulation resulting in many fresh corpora lutea. It would seem safe to assume that the injection of urines from normal pregnancies usually causes follicular rupture as well as luteinization in the ovaries of the mature rabbits.

However, the presence of ovulation points in the ovaries of the test animals is not indisputable proof of pregnancy. Correlation of the laboratory observations, recorded at the time of the tests, with subsequent clinical histories reveals that ovulation occurred as a result of the injection of urine from 12 nonpregnant individuals. Cases of real pathology, other than carcinoma, hydatidiform mole, and chorionepithelioma, yielded many of these false positives. Hence they represent limitations inherent in pregnancy tests based on the presence of gonadotropic substance in urine. Such errors are not easily remedied through laboratory management. They might be somewhat reduced in number if more complete history accompanied the specimen. Urines from patients with histories similar to those previously found to give false positive results might then be routinely subjected to testing by more than one method.

Immature rabbit tests have been used in this laboratory largely for the purpose of deciding the final report to be given in problem cases. Except in very early pregnancy, the accuracy of a mature rabbit test is doubted if the results of the immature rabbit test fail to corroborate it. A third test, by the immature female rat method, is then run. The final report is based on the results obtained by two agreeing tests. Negative tests by the immature rabbit method do not seem wholly reliable in very early pregnancy.

*Pregnancy Diagnosis by Immature Rat Tests.*—It has been found that the Davis and Ferrill<sup>22</sup> immature male rat modification is more liable to error in the hands of the technicians of this laboratory than are the methods in which immature female rats are used as test animals. The

injection of urine concentrates prepared according to Zondek<sup>23</sup> or by the method of Eberson and Silverberg,<sup>24</sup> as a means of shortening the time required for the completion of the tests, has not proved satisfactory when applied to immature female rats of our colony. Wide variations in response of the test animals is noted. Intraperitoneal rather than subcutaneous injection technic also frequently results in marked difference in the response of the individuals of a test group receiving identical doses of the urine.

**The Immature Female Rat Test:** Immature female rat tests have been run in parallel with mature rabbit tests on many of the specimens tested in this laboratory. They have been found particularly valuable in the diagnosis of pregnancies of less than three weeks' duration. Urines from such cases frequently cause so little reaction in the mature rabbit ovaries that a definitely positive report is not justified. Upon injection of the urine into 3 or more female rats of standard age and weight range, a positive reaction is usually obtained in at least one of the test animals. Aside from the fact that rats rather than mice are used, the test employed in this laboratory differs from that outlined by Aschheim<sup>25</sup> chiefly in that the urine is not injected in graded doses. Each of 3 or 5 female rats, twenty-four days old, weighing from 35 to 45 gm., is given 1 c.c. of urine by subcutaneous injection once each day for five successive days, with autopsy and ovary inspection on the sixth day. The test is considered positive if the ovaries of at least one test animal show one or more definite corpora lutea and weigh 20 mg. or more. Blood points usually appear but occasionally they are not present in ovaries of rats injected with urines of low hormone concentration. In the diagnosis of pregnancy, as well as in establishing the minimal effective dose of pregnancy urine, as described in an earlier publication,<sup>8</sup> it seems less essential that the rats be litter mates than that they be of uniform age and weight.

Of this series 9 cases, in which the results of the mature rabbit test were indeterminate or were slightly suggestive of positive reaction, were correctly diagnosed by means of the immature female rat test. Three of these were cases of pregnancy of less than three weeks' duration, and 6 of them were in nonpregnant patients. The larger number of animals in the immature female rat test group probably accounts for the more definite final result. The difficulties of housing and feeding make the use of several rabbits per test impractical; hence check tests by the immature female rat method are of value in questioned cases.

#### SUMMARY

Problems encountered in the application of the Aschheim-Zondek principle to pregnancy diagnosis in more than 800 cases are discussed. Technical details which have contributed to the simplification of several published methods and to their adaptation to the requirements of a practical and accurate clinical test method are presented.

A modification of the Friedman rabbit ovulation test is described whereby the results may be read twenty-four hours after injection of the test urine. Operative procedure for exposure of the ovaries by way of a lumbodorsal approach permits the use of a mature rabbit for from eight to twelve tests and requires but little time, technical skill, or

laboratory equipment. The criterion for judgment of test results is based on a comparison of the ovarian picture characteristically produced by injection of urines from normal pregnancies with that observed to follow injection of urines from abnormal pregnancies and from cases of endocrinopathy in the nonpregnant.

Immature rabbit and immature female rat tests are advocated for use as adjuvants of the mature rabbit test when the results of the latter are indeterminate or unusual, and also as a means of reducing the number of false positives in problem cases in which there is a demonstrable quantity of gonadotropic hormone in the urine.

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**Black: Chorionepithelioma of the Uterus, *Am. J. Surg.* 20: 651, 1933.**

The author suggests that a uterine hemorrhage, or a blood-tinged discharge following pregnancy (especially a hydatidiform mole) with a positive Aschheim-Zondek test, should arouse suspicion of a chorionepithelioma. While 45.7 per cent of chorionepitheliomas follow moles, only about 1 per cent of moles are followed by chorionepithelioma; therefore, a hysterectomy or large doses of radium are not justifiable in young women with moles. The diagnosis of typical cases of choriocarcinoma from the histologic findings and clinical symptoms should not be difficult. A panhysterectomy should be performed when a diagnosis is made, which should be followed by irradiation. As embryonic cells are very sensitive to radium rays, radium is a good prophylactic and curative agent in chorionepithelioma in selected cases. Repeated Aschheim-Zondek tests following moles and especially following hysterectomy for chorionepithelioma are of paramount prognostic importance. Patients with mole pregnancies should be watched for several months. However, if an Aschheim-Zondek test is negative, one may feel reasonably assured of no further trouble.

J. THORNWELL WITHERSPOON.

## URETERAL OBSTRUCTION IN CARCINOMA OF THE CERVIX\*

LEO S. DREXLER, M.D., F.A.C.S., AND WILLIAM E. HOWES, M.D.,  
NEW YORK, N. Y.

*(From the Brooklyn Cancer Institute, Dr. Ira I. Kaplan, Director)*

THOSE patients referred to this clinic with carcinoma of the cervix exhibit as a rule the advanced type of malignant lesions. In most instances radical surgery, radiotherapy, or a combination of both have already been instituted. They are cases that have been considered apparently cured or improved and now return with symptoms that seem unmanageable. Martin and Rogers, in gathering statistics chosen from large radiation clinics, have estimated the average five-year cures as 17.05 per cent, leaving about 83 per cent to succumb to the disease at the end of that interval. Our study deals with the management of this advanced group.

In reviewing twenty-seven consecutive autopsy records of carcinoma of the cervix in patients who died on our service, we found that ureteral obstruction with an associated ureteral dilatation and renal destruction occurred in twenty-two cases with death from uremia or chronic urinary infection. Only five patients survived to the point where distant metastases had the opportunity to develop.

When these patients came to us for examination and treatment, the usual foul-smelling discharges and in most cases the bleeding associated with cancer of the cervix had already been well controlled by previous treatment. Posterior extension and invasion of the rectal wall, with localized pain, obstipation, tenesmus and rectal bleeding were present in many instances.

Cystoscopic examination is employed in these cases to differentiate the carcinomatous invasion of the bladder wall from an irradiation cystitis. In the former one sees a marked elevation of the trigone with the mucosa reddened, but entirely intact; should bulbous edema be present, invasion has probably already occurred. In the later stages large masses of bulbous edema with areas of ulceration, papillary projections, and eventually the formation of vesicovaginal fistulas are commonly seen.

As a rule, the great majority of our patients present themselves with definite signs and symptoms of lateral extension to the broad ligaments and with ureteral obstruction. The suffering in this type of case is most intense and the outcome, of course, definitely fatal.

\*Read before the Brooklyn Urological Society, November 14, 1933.



In our study of 50 cases of carcinoma of the cervix with broad ligament extensions, it was our chief aim to determine what could be accomplished by intensive treatment directed to this area. In every case the chief complaint is pain, ranging from a dull ache to a severe colic on the affected side. Usually the patient complains of a constant dull pain located deeply in the groin and referred to the thigh and leg, often simulating an attack of sciatica. At times the pain is referred to the sacrum, simulating sacroiliac disease. The pain is frequently referred to one or both kidneys, especially when complete occlusion of the ureter has taken place with dilatation of the ureter and renal pelvis above the point of obstruction. When infection secondary to ureteral obstruction and its associated urinary stasis occurs, chills and fever commonly appear with anorexia, general malaise, and prostration. The urine in the infected hydronephrosis is often purulent, at times containing an appreciable amount of blood. When the ureteral occlusion is unilateral, the urine is often persistently clear, although definite evidence of a large infected hydronephrosis is present. Gastrointestinal symptoms are always pronounced and are often disturbing. They arise from reflex disturbances, toxic absorption, or from pressure and irritation to the parietal peritoneum. Marked gaseous distention, belching, nausea, and vomiting are commonly the complaints. Rectal tenesmus and diarrhea are occasionally noted, simulating an attack of colitis, or even rectal invasion of the malignancy itself. This type of patient often develops a marked distaste for food but with removal of the ureteral obstruction the appetite returns, and the gain in weight is rapid, in some instances from 10 to 100 pounds.

On physical examination through the rectum, a moderate degree of induration, which is tender to the touch, can be felt extending laterally. Cystoscopy with ureteral catheterization and pyelography establishes a positive diagnosis. Of the 50 patients cystoscoped, 34 showed evidence of hydronephrosis, in 18 occurring on the right, in 10 on the left, and in 6 cases both sides were involved to a greater or lesser degree. In every case there was evidence of ureteral narrowing or complete obstruction with a corresponding dilatation above the point of obstruction. In all cases the obstructions were in the terminal portion of the ureter.

#### ETIOLOGY AND MECHANISMS OF URETERAL OBSTRUCTIONS

Although ureteral involvement with its associated hydronephritic changes in carcinoma of the cervix is a well-recognized entity, there has been a great amount of discussion as to the actual mechanism of obstruction as well as to the etiologic factors that produce this obstruction. Some observers feel that excessive radiation therapy with the formation of reactive scar tissue is the important factor in the

formation of these strictures. All our patients had received some form of irradiation. Thibaudeau, however, has reported cases where no radiation therapy had been given, but at autopsy a bilateral hydronephrosis was revealed with both ureters markedly dilated. In one case with unilateral obstruction we explored the lower ureter and found it buried in a mass of fibrotic tissue. A section of this tissue was removed and was found to be definitely carcinomatous in nature. Martin and Rogers, in investigating the effect of radiation therapy on the ureter, applied radium capsules directly to the ureter and studied the effects of 1.5 and 2.5 erythema doses on the ureters. In no case was any stricture of the ureter produced and pyelograms performed after the kidney and ureters had been removed showed no evidences of hydronephrosis. They concluded that inasmuch as only about  $1/5$  erythema doses of filtered radiation reach the ureter, stricture formation would be most unlikely. Metastases into the lymphatics of the ureter have been described, as well as invasion of the ureteral wall itself, though such conditions may be considered as rare. From our autopsy findings we feel that these strictures are definitely the result of pressure on the ureter from invasion of the broad ligament by the malignant process itself. Based on this fact we deem it necessary to direct therapy to this area with the same vigor as the primary lesion in the cervix has been attacked.

The method of attacking carcinoma of the periureteral structures from a radiologic standpoint is the same as that used in treating advanced carcinoma of the cervix.

First, x-ray therapy is administered to the pelvis through four or five large ports. If an additional perineal port is used, this is usually of small size. One of the methods employed has been that of the saturation technic as worked out by Kingery and by Pfahler. The surface dose is varied from 90 to 120 per cent in an attempt to get a previously calculated amount into the midpelvic area. Another method is to give 100 per cent skin erythema dose to one port daily until four or five areas have been treated giving a total of from 3,000 to 6,000 R units. Immediately following the x-ray therapy, usually within one week, radium is applied by means of small doses well filtered over a long period of time as suggested by Regaud at the Currie Institute. For this we employ the modified colpostat and cork devised and described by Kaplan, using from 10 to 15 millicuries of radium in each applicator, or a total of from 60 to 90 millicuries, filtered through  $1\frac{1}{2}$  or 2 mm. of platinum, plus 1 cm. of rubber in the vagina. A sound containing three tubes of radium is inserted into the uterus. This may be done at one time, or the vaginal application at one session and the uterine at another, depending on the local condition present. The radium is applied over a period of from four to six days. The tubes are maintained in position by careful vaginal packing with iodoform gauze for the whole period of the treatment. This method differs from that of Regaud in which the radium application is removed and cleansed daily; we have found the removal of radium and packing a painful procedure and the reinserting without an anesthetic even more so. In our service unusually few complications have occurred. Great care is taken to keep the bladder and rectum emptied during this period of radia-

tion. A total dose of from 5,000 to 6,000 mc. hr. is given, usually about 3,000 intra-uterine and 3,000 or more intravaginally.

Up to the present time no satisfactory radiation therapy has been devised for the broad ligament and parauterine malignant extension. Cohen suggests the insertion of radium needles into the periureteral tissue through a laparotomy opening. Capillary glass radon tubes are suggested by others for this purpose, and more favor insertion of needles into the parametrium via the vagina. From the experimental work of Martin and Rogers, it would appear that the insertion of radium needles into the broad ligament areas is not a safe procedure because this in itself produces obstructive changes in the ureter unless preliminary transplantation of the ureters has been done.

Our most satisfying results, however, were obtained not from radiation but from ureteral dilatation. The ureters were dilated about every fourteen days with the instillation of 1 per cent silver nitrate into the kidney pelvis. In many cases catheterization was at first difficult but filiform bougies eventually were passed by the point of obstruction. These were allowed to remain in situ for forty-eight hours and then followed by larger bougies or catheters. In the presence of infection, especially with marked elevations of temperatures and large amount of infected residual urine in the pelvis, the catheters were permitted to remain in situ for drainage for several days. In two cases in which the infection was not controlled nephrectomy was necessary. Both of these cases did exceptionally well following removal of the kidneys. Although we have transplanted the ureters to the sigmoid in two of our cases, we feel that this procedure is too hazardous, for this type of patient is usually already in poor condition. However, implantation of the ureters into the loin causes little added shock or risk and is technically much simpler to carry out. We intend to continue this procedure in the future where bilateral ureteral obstruction exists and where ureteral dilatation has failed. We have found that with routine ureteral dilatation a great many of our cases have been greatly relieved of their pain, so much so that a number have been able to dispense with narcotics. The usual interval between dilatations is about two weeks.

In 2 cases definite unilateral complete obstructions were found associated with severe pain and infection. Repeated attempts at ureteral dilatation were unsuccessful and nephrectomies were performed in both instances. In 3 cases, although the obstructions could be overcome, the infection could not and removal of the affected kidney was decided on and successfully performed. In one case a complete obstruction of one ureter with a partial obstruction on the other side and severe infection was found. In this case transplantation of the ureters in the loin was performed. Almost immediate improvement followed and the patient was discharged from the Institute after having previously been bedridden for many weeks in constant pain and on the verge of death from uremia. Of the remaining 5 patients with bilateral involvement 2 have died, and 1 refused operation and left the hospital improved. Two patients are still under observation, having improved somewhat with ureteral dilatation. Those with unilateral involvement are being dilated cystoscopically and watched for renal infection and loss of renal function.

#### CASE REPORTS

CASE 1.—L. L., white, aged thirty-eight years, was admitted March 23, 1932, in poor physical condition, complaining of severe pain in the right lower quadrant. She gave a history of pronounced vaginal bleeding which began in December, 1930. She had had a uterine suspension in 1929. The patient had been previously admitted to our service on January 21, 1931, with a large eroded ulcerated cervix. Biopsy report at that time showed the presence of an anaplastic epidermoid carcinoma of the cervix. There were marked digestive disturbances and a loss of 20 pounds in

weight. In February, 1931, she received x-ray therapy, a dose of 3,440 r. units, through four portals of the pelvis repeated daily for four days. On February 5, 1931, a three-cork radium colpostat and a uterine sound containing 102 mc. were inserted in the vagina and uterus for three days and eighteen hours, giving a dose of 6,000 mc. hr. filtered through 1 mm. of platinum. Bleeding was controlled, but the patient's general condition remained poor. She had a marked distaste for food and a constant loss of weight and strength. She also complained of a pain in the right lower quadrant. Some time later she was returned to the hospital with a diagnosis of acute appendicitis. We saw her in consultation and found the vaginal canal contracted so that the cervix could not be explored with the ordinary speculum. The cervix was definitely indurated, but there was no bleeding on manipulation. The uterus was fixed to the anterior abdominal wall and slightly enlarged. The right parametrium was very tender. In our opinion the right parametrium was involved as an extension from the cervical malignancy. Cystoscopy showed a normally appearing bladder mucosa, and there was no evidence of vesical encroachment. The left ureter was catheterized to the kidney pelvis and the delivered urine was clear. In the right ureter an obstruction was met about 3 cm. from

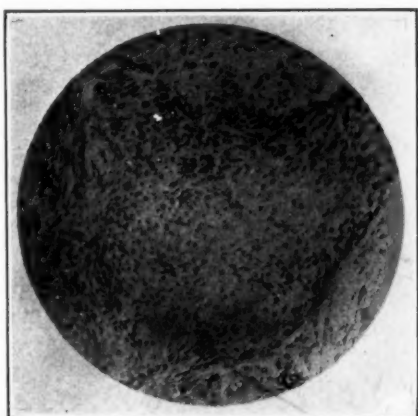


Fig. 1.

Fig. 1.—Case 1. Section from tissue at the point of obstruction, reported as epidermoid carcinoma.



Fig. 2.

Fig. 2.—Case 2. Retrograde pyelogram showing definite evidences of renal destruction.

the vesical orifice. This could not be passed by. Indigo carmine injected intravenously returned in four minutes on the left side. There was no return of the dye at all on the right side at the end of thirty minutes. Pyelography revealed a rather normal kidney pelvis and ureter on the left, on the right no sodium iodide would go past the point of obstruction and regurgitated back into the bladder. Intravenous pyelography showed a normal pelvis and calices on the left with no visualization on the right. X-ray of the bony pelvis showed no evidence of neoplastic metastases.

Hemoglobin content was 62 per cent; red cells, 4,050,000; white cells, 8,000; polymorphonuclears, 82 per cent; lymphocytes, 16 per cent; mononuclears, 2 per cent. She was found to be Type III. Blood chemistry showed no abnormal findings.

As the patient's condition was becoming progressively worse and the intense pain on the right side continued, surgical exploration was decided upon and carried out May 18, 1932. A right anterior incision was made and the ureter explored extraperitoneally. The right ureter was greatly dilated, and following it down to

the point of obstruction, we found it embedded in a mass of carcinomatous tissue. A section of this tissue was removed with the lower ureter. The patient was then turned on her side and the kidney explored. The tied ureter was pulled through the upper incision and a complete nephroureterectomy was performed. The removed kidney was completely hydronephritic and functionless. Section of the fibrotic tissue removed was reported as a metastatic anaplastic carcinoma extending into the ureter.



Fig. 3.—Retrograde pyelogram showing right-sided renal destruction. The left kidney was found to be normal.



Fig. 4.—Intravenous pyelogram showing a normal pelvis and ureter on the left and an absence of visualization on the right. Operation revealed a large hydronephrosis on the right side secondary to the obstruction in the lower ureter.

The postoperative course was uneventful; both wounds healed by primary intention. The patient was discharged on June 16, 1932, in good condition which has continued up to the present. Her appetite has improved, and her pain has been absolutely relieved. By April 1, 1933, she had gained 40 pounds.

CASE 2.—I. T., white, married, aged thirty-seven years, was admitted to the hospital on February 20, 1932, complaining of pain in the left groin radiating to the leg and back, chills, fever, sweats, and marked urinary discomfort. She had been under observation in the clinic since November 2, 1931. At that time she was re-



ferred for x-ray therapy from another institution, where she had received radium therapy for carcinoma of the cervix. Because of profuse vaginal bleeding she was admitted to our hospital and at the time of her admission there was a history of marked bleeding of eight months' duration with loss of weight and strength. She had had six children and one abortion. Vaginal examination showed the cervix replaced by a bleeding mass. The adnexa was not palpable and the uterus enlarged. A biopsy was taken and reported as anaplastic carcinoma of the cervix. Ambulatory treatment with deep x-ray therapy was advised and she received a pelvic cycle of 6,800 r. units within a period of three weeks. Her bleeding was controlled but her general condition became worse. There was marked anorexia, nausea, and vomiting with progressive loss of weight and a marked elevation of temperature ranging between 100° and 105° F. She complained of frequent chills, marked night sweats, and severe urinary disturbances.

The patient was again admitted to the hospital January 10, 1933.

She was poorly nourished, markedly emaciated and acutely ill. The abdomen was soft, and there appeared to be definite tenderness over both lumbar areas with some



Fig. 5.—Section of periureteral tissue showing definite evidence of carcinomatous invasion.

muscular spasticity present on both sides but more prominent on the left. The liver and spleen were not palpable. There was an x-ray erythema over the abnormal skin. The cervix was nodular but there was no bleeding on manipulation. There was some induration in the left parametrium.

Hemoglobin content was 38 per cent; red cells, 3,280,000; white cells, 21,400; color index, 6; polymorphonuclears, 83 per cent; lymphocytes, 17 per cent; blood, Type IV.

The urine was cloudy with a heavy trace of albumin and many pus cells.

Blood chemistry findings were within normal limits. A cystoscopic examination revealed evidence of a fibrinous cystitis. The right ureter was catheterized to the pelvis without evidence of obstruction. On the left an obstruction was met 3 cm. above the vesical orifice. This was overcome, and the catheter passed to the pelvis. The urine was purulent and under pressure. Indigo carmine injected intravenously returned in three minutes on the right in good concentration. No return in 30 minutes on the left. The left catheter was left in situ for drainage. Pyelography revealed evidence of a marked hydronephrosis with an associated dilatation of the ureter above the point of obstruction. A diagnosis of markedly infected hydro-

nephrotic kidney, secondary to an ureteral stricture, was made. With ureteral drainage, the temperature dropped to 100° F. After four days the catheter was removed. After removal of the catheters the temperature again went up to 104° with marked tenderness over the left kidney. Surgical intervention was decided upon and on March 14, 1933, the left kidney was explored. The kidney showed evidence of a hydronephrosis and was removed. Convalescence was uneventful.

The patient was discharged on April 10, in excellent condition. Since that time she has reported to the clinic at regular intervals. Her urinary symptoms have subsided and pain has disappeared. In July, 1933, she weighed 190 pounds, a gain of 100 pounds since the time of operation.

CASE 3.—B. R., white, aged fifty years, married, was admitted to the hospital May 8, 1933, with severe pain in the right groin radiating to the right leg, hip, and back. She had been running irregular septic temperatures for the past few weeks. There was a marked distaste for food, gaseous distention, nausea, vomiting, and generalized prostration. She had been under observation since January 19, 1932, a colpostat and cork were placed in the vagina containing 30 mc. for 144 hours totaling 2,640 mc. hr. the filtration being 1 mm. platinum. On January 25, 1932, a tandem was inserted into the uterine canal containing 53 mc. for 144 hours totaling 2,900 mc. hr. During this time she had also been given a pelvic cycle of short wave length x-ray therapy totaling 3,440 R units. She returned to clinic on May 1, 1933, complaining of severe pain in the right groin and received an additional x-ray therapy cycle to the pelvis totaling 6,400 R units. Her pain continued. She was complaining of chills and irregular temperatures. Cystoscopic examination at this time revealed an obstruction in the right lower ureter, this was overcome, and the ureter was catheterized to the pelvis. The urine was under marked pressure and purulent in character. No obstruction was met in the left and the urine appeared to be clear. Indigo carmine injected intravenously returned in four minutes on the left and in good concentration, while only a poorly concentrated dye appeared on the right side at the end of twenty-five minutes. Bilateral pyelography revealed the presence of a hydronephrosis on the right side with a markedly dilated ureter extending to the point of obstruction. The left ureter was normal in appearance and the renal pelvis was only slightly dilated.

On admission to the hospital a catheter was passed to the right pelvis and allowed to remain in situ for four days. The pelvis was irrigated every three hours.

Following the withdrawal of the catheter the temperature again rose to 103° F. with severe pain on the right side. Surgical exploration was decided upon and on June 8, 1933, a right nephrectomy was performed. The kidney showed definite evidence of an infected hydronephrosis. She made an uneventful recovery and was discharged on July 1, 1933. She was last seen on Sept. 15, 1933. The pain had entirely disappeared. Her general condition was greatly improved, her appetite was good and she had gained 15 pounds and was able to attend to her household duties.

CASE 4.—F. G., aged fifty years, was admitted to the hospital on May 1, 1933, complaining of severe pain in both groins radiating to the hip and back, irregular temperatures, anorexia, loss of weight, and a leakage of urine through the vagina. Her first admission to the hospital was on April 19, 1932. At the time she had profuse vaginal bleeding and stated then that she had been in good health until the onset of vaginal bleeding in July, 1931. There were no severe illnesses or operations. She had three children, all alive, no miscarriages. Her menstrual history was normal, periods beginning at fifteen years, occurring every twenty-eight days, and lasting four days. Menopause at the age of forty-six years. During July, 1931, she bled rather profusely from the vagina and was referred to another hospital. The pathologic report at that institute was advanced carcinoma of the

cervix, Grade II, relatively radio resistant. She received a high voltage x-ray therapy cycle to the pelvis of four exposures over the anterior and posterior areas, receiving 700 r. units at each treatment.

Because of her condition she was referred to the Brooklyn Cancer Institute for further care, on March 16, 1932; here she received x-ray therapy to the pelvis totaling 5,000 r. units. On April 8, 1932, a tandem and cork were inserted into the uterus and vagina, respectively, containing 40 mc. for 102 hours, a dose of 2,840 mc. hr. was given. On April 21, 1933, a tandem and cork were again inserted containing 40 mc. for a dosage of 1,510 mc. hr. On June 16, 1932, the pelvis was again treated with x-ray therapy giving a total of 5,160 r. units. November 18, 1932, a similar course of deep x-ray therapy treatments was instituted totaling 5,160 r. units. January 2, 1933, this pelvic cycle was again repeated for another total of 5,700 r. units. Her general physical condition was fair. No masses were palpable in the abdomen. Both kidneys, however, were definitely palpable and there was marked costoureteral tenderness.

Her vagina was narrow and contracted, and the cervix was markedly ulcerated. Rectal examination revealed marked tenderness and evidence of induration in both parametria. Her blood count showed a red count of 3,400,000, with a hemoglobin of 60 per cent and a leucocyte count of 6,000. Blood sugar was 90 mg. Cystoscopy revealed the presence of a vesicovaginal fistula with a marked elevation of the trigone and evidence of bulbous edema on the floor of the bladder. A cystogram disclosed the presence of a filling defect on the posterior wall showing definite evidence of secondary infiltration. An intravenous pyelogram revealed a functionless kidney on the left and a marked dilatation of the right pelvis with a large atonic kinked ureter. The patient was in extreme pain, constantly wet; she pleaded with us to do something surgically that might afford her some relief.

Transplantation of the ureters to the sigmoid was decided upon and on May 11, 1933, using Coffey's tube technic, the left ureter was transplanted into the sigmoid. Her condition did not permit the bilateral transplantation that we had hoped could be performed at this time. She made a surprisingly rapid recovery and asked to be discharged from the hospital before undergoing the second operation. She was discharged on June 5, 1933, and on July 3, 1933, she returned much improved; on July 6 a right rectal incision was made and the peritoneum opened. The sigmoid was found fixed by firm adhesions to the pelvis and uterus. The posterior peritoneum was opened on the right side. The right ureter was easily isolated and found to be greatly dilated in its lower portion and buried in a mass of malignant tissue. The ureter was clamped and cut above the point of obstruction. However, it was found that the ureter could not be brought down to the sigmoid without a great amount of tension. A stab wound was made in the skin and the ureter brought out into the loin. The posterior peritoneum and the abdomen were then closed and the ureter fixed to the skin. A number 12 catheter was inserted into the pelvis for drainage. She again made a rapid recovery and was discharged on August 5 wearing a collecting receptacle on the right side. She is now almost completely free from pain, her appetite improving; by September 15 she had gained 8 pounds since the time of her admission to the hospital.

#### SUMMARY

The intense suffering of patients with carcinoma of the cervix late in the disease is caused in almost every case by broad ligament extension with ureteral obstruction. This process progresses until complete obstruction of the ureters, secondary renal infection, and death from uremia have occurred. A summary of the treatment directed

to 50 cases of this type illustrates very definitely that a great deal can often be accomplished when the condition is recognized and treatment is directed to this area. Repeated cystoscopies and pyelograms are most important in the follow-up treatment of carcinoma of the cervix so that extension to the ureter can be recognized early and treatments instituted. It has been felt that a fibrotic contracture of the tumor cells following x-ray and radium therapy is responsible for the encroachment on the ureter. This does not appear to occur any more frequently now than before the advent of x-ray and radium therapy. The encroachment to the ureter is usually an active cellular proliferation and is seldom demonstrated as any bad result of post-radiation fibrosis.

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### A PLEA FOR THE ALEXANDER METHOD OF SHORTENING THE ROUND LIGAMENTS FOR RETROVERSION OF THE UTERUS\*

LOUIS J. LADIN, A.B., M.D., F.A.C.S., AND JOSEPH O. SMIGEL, M.D.,  
NEW YORK, N. Y.

(From the Department of Gynecology, New York Polyclinic Medical  
School and Hospital)

OF ALL the operations for shortening the round ligaments for retroversion devised and practiced to date, there is none in our belief that compares with Alexander's method in efficiency and in immediate and remote results. It is a simple and safe procedure, based on sound anatomical grounds, and is easy of performance. In this operation the fundus uteri is kept forward and freely movable and is not abnormally suspended; the cervix is held back, and the ovaries and tubes remain normally suspended and free from mechanical interference; there are no extraneous elements and plications and no distortions of the pelvic organs; the operation leaves the uterus and adnexa in a perfectly normal anatomic and physiologic condition. Moreover, the strongest parts of the round ligaments are utilized; the stretched and slack portions are removed; and the normal function of the ligaments is restored.

Why has this feasible, most effective, and ideal operation fallen into undeserved disrepute? The reason can be traced to two objections which were apparently insurmountable in former years.

\*Read at a meeting of the Clinical Society of the Polyclinic Medical School and Hospital, January 8, 1934.

The one obstacle to the general adoption of the method, both in the early days and at the present time, is due to the faulty description of the technic for finding and drawing out of the ligament, as described by Alexander in 1884. This was mainly responsible for making the operation difficult and uncertain, even in the hands of capable surgeons. The modifications suggested by the other advocates of the operation were of no greater help to the inexperienced.

As evidence of this it would be well to quote from an article by Dr. Le Roy Broun<sup>2</sup> of the Women's Hospital, New York:

I know of no operation in gynecological surgery in which minute detail is of so much importance as in the performance of this operation; nor do I know of any in which the recognized surgical ability of the operator is of so little assistance to him in his first cases.

We are in absolute accord with this statement.

To overcome these difficulties, Dr. Broun offered a new procedure which, in his opinion, rendered the operation one of ease and certainty. We will not go into the Broun technic, for the reason that while it was an improvement on the description of Alexander and was apparently satisfactory to a surgeon who had had large experience with this operation, it was of no real value or assistance to those who had no experience with the operation.

In spite of the efforts of Dr. Broun and other enthusiastic advocates to popularize Alexander's operation, it continued to fall into disuse, and for no other reason than the supposed technical difficulty associated with its performance.

The other important and very serious objection to Alexander's operation was its extraperitoneal character. This was obviously well founded and justified. It stands to reason that original Alexander's operation, uncombined with laparotomy, which it was never intended to replace, did not permit intraperitoneal exploration and necessary pelvic surgery; this led to errors in diagnosis, and the operation was performed in many cases where it was absolutely contraindicated. In consequence, many failures were attributed to the operation, instead of to mistakes in diagnosis, in overlooking, at the time of operation, the presence of adnexal disease or adhesions.

The original extraperitoneal Alexander's operation was only indicated in freely movable and uncomplicated retroversions of the uterus, and was never intended to relieve adhesions, cure adnexal disease, or other pelvic pathology. It never should have been undertaken where bimanual palpation did not positively eliminate the presence of these complications, or even when the diagnosis in this respect was in doubt.

In order to eliminate the objectionable extraperitoneal feature, which was largely responsible for putting Alexander's operation into the discard, surgeons who approved Alexander's method combined it with abdominal section, either through a midline or Pfannen-



stiel incision. Thus among others, Skene Keith,<sup>3</sup> in 1900, R. Peterson<sup>4</sup> in 1906, in Germany, Werth,<sup>5</sup> Kuestner,<sup>6</sup> Littauer,<sup>7</sup> and Broese<sup>8</sup> in 1909, and again in this country Barton C. Hirst,<sup>9</sup> in 1910 and Le Roy Broun,<sup>10</sup> in 1911 recommended combining Alexander's operation with opening the peritoneal cavity. Goldspohn<sup>11</sup> in 1911 described an "Intra-peritoneal Shortening of the Round Ligaments Through Temporarily Dilated Inguinal Canals and Internal Rings."

Notwithstanding the fact that the combined operation made Alexander's operation available for all cases of retroversion either with or without complications, only a comparatively few operators practiced it, among whom may be mentioned John C. Hirst of Philadelphia. He followed until recently the method introduced by his father in 1910, namely, combining through a Pfannenstiel skin incision Alexander's operation with laparotomy. In an article published in 1930 Dr. Hirst<sup>12</sup> advocated combining Alexander's operation through incision in the groin with a laparotomy through a midline incision. He chose this method notwithstanding the three incisions because he regarded it superior to all others.

The function of the round ligaments is to serve as stays and guy ropes in maintaining the uterus in the anteverted position, as is evidenced by the fact that when the ligaments are undeveloped or absent, there is congenital retroversion; and when they remain subinvolved or unduly stretched and lengthened after pregnancy and delivery, acquired retroversion is the result. As the normal attachment of the round ligaments is at the external inguinal rings, we fully agree with Dr. Hirst that the most logical approach for shortening them is through the external rings, even though it may be necessary to add a small skin incision in each groin.

As to the question of a possible incisional hernia at the groin, the sewing in of the proximal end of the ligament into the external ring and canal, in the absence of infection, will not result in hernia; on the contrary, it will cure a possible tendency toward its development.

The introduction of the procedure of combining Alexander's operation with abdominal section removed the only real and justified objection to it. But in spite of this, the procedure failed to receive the general recognition it so richly deserved, unquestionably because of the supposed imaginary difficulty in finding and withdrawing the ligaments from the inguinal canals.

As a consequence numerous intraperitoneal procedures were devised and practiced for shortening the round ligaments, not one of which has become standard.

It is needless to enter into a description and discussion of even the most important of the multiplicity of operations that have been recommended and employed for retroversion of the uterus; it is sufficient

for the purpose of this plea to enumerate a few of them in order to indicate the various and diverse methods that are in vogue.

For example: In Olshausen's operation and in Gilliam's operation and its various modifications, the uterus is suspended from the abdominal wall by means of the round ligaments. Among the different intraperitoneal plication operations the following are the most important: In Wylie's the ligaments are plicated and sutured into the broad ligament; in Coffey's, the round ligaments are plicated and sutured to the anterior and lateral walls of the uterus; in Baldy-Webster's, the round ligaments are plicated posterior to the uterus, and in Dudley's, the round ligaments are plicated in front of the uterus.

Objections have been raised from time to time by various operators and authors to every one of the intraperitoneal plication operations, and especially to ventral suspension and fixation, among which are the following: In ventral suspension the uterus is fixed in an abnormal position; there are one or more pillars between the uterus and the abdominal wall causing, at times, internal hernia and intestinal obstruction; pregnancy and delivery may be interfered with. In plications, the weak end of the round ligament is depended on for support; the motion of the uterus is limited; the suspension of the ovaries is distorted, and they are frequently imbedded in adhesions; the sigmoid may become adherent to the uterus; intestinal adhesions may form at the suture lines, and there is a tendency toward thrombosis of the pelvic veins.

An illuminating argument against the intraabdominal plication and suspension operations is the statement of Wollner.<sup>13</sup> In a report of 100 consecutive cases by the modified Gilliam method, published in 1932, he found in a careful follow-up, that in approximately 60 per cent of these cases, the operation failed to bring about the subsidence of the symptoms of backache and abdominal pain.

This is in accord with the experience of other surgeons and with our observations of private and clinic patients who have been operated upon previously, by one or another of the above methods. We agree absolutely as to the results, but we cannot subscribe to the theory that the postoperative failures are due to causative factors other than the maladjustments of the pelvic organs resulting from the various methods of plicating the round ligaments or suspending the uterus.

To overcome some of the above objections, especially the elimination of peritoneal adhesions, and to produce a condition that would more nearly simulate nature, modifications for shortening the round ligaments have been devised by Simpson, Montgomery, Neal, and Mayo, having for their object, an approach to the extraperitoneal method of Alexander by the creation of an artificial canal for the round ligaments, located subperitoneally or retroperitoneally.

In contrast with all the other procedures it is well to emphasize the fact that none of the above objections can be charged against Alexander's operation. Moreover, there are no other justified or reasonable objections whatsoever. The argument against it on the ground of its being an extraperitoneal operation has been entirely refuted by the introduction of the combined operation; and the imaginary difficulty and uncertainty in finding and withdrawing the ligaments at the external ring can be readily overcome by following the description of the procedure and technic as practiced by us.

Notwithstanding opinions to the contrary, it was the conviction of the senior author that retroversion of the uterus, even when simple and uncomplicated, does produce symptoms, and he has invariably advised operation for this condition.

The results of the large series of the Alexander operations performed by him, whether by the extraperitoneal method with incisions in the groins or combined with abdominal section through a Pfannenstiel incision, were most gratifying and permanent. Many of the patients have subsequently conceived one or more times and were delivered without any complications resulting from the operation.

As it is universally conceded that shortening of the round ligaments, in some form or other, is the only adequate surgical procedure for retroversion of the uterus, statistics and follow-ups have been omitted purposely in order not to befog the main object and purpose of this paper, namely, to prove by this appeal that Alexander's is by far the very best method.

It must be clearly understood that shortening of the round ligaments either by Alexander's or any other method cannot and will not accomplish anything beyond the correction of the retroversion. Complications must be treated according to the requirements. In the presence of adhesions, adnexal diseases, or other pelvic pathology, laparotomy must be added. For descensus uteri, cervical pathology and vaginal relaxation, shortening of the ligaments must be supplemented by vaginal plastic surgery.

In the early descriptions too many landmarks were given, and too much stress was laid on details which only served to confuse rather than elucidate the ease with which the ligaments can be found.

In our technic, the one landmark, and the only landmark that is used throughout the entire manipulation, is the spine of the pubis. The other precautions are to cut cleanly through the skin, down to the aponeurosis of the external oblique, care being taken not to confuse the external fascia with the aponeurosis.

The external ring is not always palpable through the skin, or through the incision, especially in fairly stout patients, but the spine of the pubis can invariably be felt in every patient. It is a knob or

projection about three-eighths of an inch in size, situated on the outer part of the upper border of the crest of the pubis. The external ring is always situated immediately above and to the outer side of the spine of the pubis.

The spine is the fixed point that is to be used and depended upon as the guide before making the incision through the skin, for locating the external ring, and after the skin is incised, for exposing the ring and for finding and withdrawing the ligaments.

#### TECHNIC

In the external operation an incision of about two and one-half inches is made through the skin in either groin, extending upward on an imaginary line running from the spine of the pubis to the spine of the ileum, that is, along the course of the inguinal canal.

With the spine as a constant guide, short subsequent incisions are made down to the fascia. The tissues, consisting of superficial and intercolumnar fascia, immediately above the ring must be dissected bluntly until the glistening border of the inner and outer pillar is exposed; great care must be taken not to distort the tissues, either by retraction of the wound or by cutting into the fibers of the aponeurosis of the external oblique.

With the spine as a guide the ring is felt and the glistening edges of the pillars are freed by blunt dissection of the superficial fascia. The entire contents of the inguinal canal, between the pillars of the external ring, down to the periosteum of the pubic bone are grasped en masse with mouse tooth forceps and lifted out of the canal, and a clamp placed underneath. The contents of the ring consist of the fan-shaped insertion of the round ligament, fat, vessels, and nerve. No attempt is made to separate them before they are lifted out, to avoid tearing and destroying the insertion.

After separating the nerve, the lifted out portion is clamped by two smooth clamps and is divided between them (ordinary artery clamps filed off or tipped with rubber tubing are used). The distal end is tied with a plain ligature and the clamp removed; the proximal end, that is, the insertion of the ligament and vessels, is twisted around the end of the clamp, and gradually and very slowly teased and drawn out of the canal—there must be no forcible pulling out of the ligament. At times when the retroversion has existed for a long time, the ligament may be held down by adhesions. These are readily freed by retracting with a wet sponge or by blunt dissection. The ligament is withdrawn until the peritoneal reflection of the round ligament comes into view, or until there is no give to it.

The ease and facility of the operation depend on the correct identification and use of the one important landmark, namely, the pubic spine, and on minute attention to the above described dissection and technic.

Both in the simple Alexander operation and when combined with laparotomy, the inguinal canal is not opened up at all. If, however, the ligament should break on traction because of its thinness, friability, or adherence, the anterior wall of the canal is slit up, and the round ligament picked up higher in the inguinal canal. This will be found necessary only on rare occasions.

The ligament is sutured to the canal in the following manner: While the ligament is held taut, four or five interrupted chromic sutures are passed through the ligament and through the inner and outer pillar of the ring, the lowermost suture including the periosteum. The sutures are not tied until they are all passed. They are then tied and cut, and the slack of the ligament cut and removed. The wound is closed with continuous catgut suture, and one silkworm retention suture.

In the combined Alexander with laparotomy, the procedure for shortening the ligaments is exactly identical with that of the extraperitoneal method, except the skin incision. Here also the spines of the pubes are used as guides and landmarks to expose the external inguinal rings, and the insertion of the ligament is grasped and withdrawn in accordance with the description above.

In the combined operation, when the shortening of the round ligaments is decided on before opening the abdomen, the skin incision consists of a transverse or modified Pfannenstiel. When it is necessary to shorten the ligaments after the abdomen has been opened through a median incision, the skin incisions in the groin are then added. In the transverse skin incision, the lower skin flap is retracted until the spines of the pubes are felt and the external rings are exposed. The upper skin flap is dissected up for about three inches, and the abdominal cavity is opened through a median longitudinal incision including fascia, muscle, and peritoneum, and the necessary surgery is done in the pelvis. The round ligaments are shortened and sutured as above, and the abdominal incision is sutured in layers. The skin incision is then closed with catgut, and several silkworm retention sutures.

#### SUMMARY

Most of the other operations for retroversion so far devised have for their aim and purpose the shortening of the round ligaments, either subperitoneally or intraperitoneally. In Alexander's operation, however, the shortening is accomplished extraperitoneally; this in itself is a decided advantage. In cases requiring pelvic surgery Alexander's operation is combined with an abdominal section through either a median incision with two skin incisions in the groins or through one Pfannenstiel, or transverse skin, incision.

It is true that the extraperitoneal character of the original Alexander operation was a real and justified objection, but it is equally true that this objection had been removed over twenty years ago by the combined method, and yet this illogical and ill-founded argument is still used against Alexander's operation. As an instance we wish to cite a recent article, *The Operative Correction of Uterine Displacements*, by Dannreuther,<sup>14</sup> in which he arrives at the following conclusions:

The Alexander-Adams Operation should be relegated to the background forever. It requires two incisions in the abdominal wall instead of one, affords no opportunity for intraperitoneal exploration, is sometimes attended by technical difficulties when the round ligaments are thin and hard to find in the inguinal canal, and carries a high percentage of unsatisfactory results.

Unfortunately the above opinion in regard to Alexander's operation is the generally accepted view, and we are offering this plea on behalf of the operation, with a view and in the hope of modifying this attitude on the part of operators.

Instead of relegating this operation to the background, it should be made the standard operation for the shortening of the round ligaments. By the use of the Pfannenstiel incision, only one skin incision is required and, moreover, the two groin incisions are only skin incisions and not abdominal incisions. By following the description outlined



here, technical difficulties in finding the ligaments will seldom be met, and the combined operation does permit intraperitoneal exploration and surgery when necessary.

It is paradoxical that an unnecessary multiplicity of operations should have been successively devised for so simple a procedure as shortening of the round ligaments, every one of which was, in view of the innumerable modifications, obviously unsatisfactory in one respect or another. On the other hand, the operation introduced by Alexander nearly fifty years ago, which is beyond any doubt or question safe, logical, reliable and effective, easy of performance, if a satisfactory technic is followed, and applicable in all cases, except congenital retroversion, instead of becoming the standard, has been generally rejected.

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1289 MADISON AVENUE

**Owen, May: A Case of Sarcoma Botryoides, J. Lab. & Clin. Med. 18: 497, 1933.**

The author reports a case of this rare tumor, occurring in a negro child four years of age, with recurrence and death two and one-half months after previous surgical removal. Two months previously she had had a vaginal operation for removal of a large tumor, which latter had not been submitted for pathologic examination.

While in the hospital, bladder catheterization and irrigation and vaginal douches were necessary throughout her stay. She died three weeks after admission. Postmortem examination: the uterus and bladder formed a large lobulated mass reaching to the umbilicus; the bladder mucosa was thick polypoid and edematous. The body of the uterus was the size of an adult's and contained thick purulent fluid; it had a granular brownish red necrotic lining; the uterine wall was thin, averaged 5 mm. The vagina was enlarged and contained a thick foul-smelling liquid; its lower 9 cm. contained an edematous soft papillary tumor attached to the posterior wall. Secondary pathologic findings were pelvic peritonitis, hydronephrosis of right kidney and central necrosis of the liver. Microsections showed the tumor composed chiefly of loose cellular fibrous tissue, scattered through which were a few smooth and striated muscle fibers. The more superficial portions were diffusely infiltrated with inflammatory cells. Sections from the less edematous areas of the tumor showed a few large cells that had large, oval slightly elongated, hyperchromatic nuclei.

W. B. SERBIN.

## INFREQUENT COMPLICATIONS OF UTERINE CANCER, WITH CERTAIN CLINICAL OBSERVATIONS\*

LEWIS C. SCHEFFEY, M.D., PHILADELPHIA, PA.

(From the Department of Gynecology, Jefferson Medical College Hospital)

IN THE ordinary compilation of data relating to the problem of uterine cancer, the major part of the presentation is fundamentally a group study. Frequently, however, time and space do not permit of a discussion of the individual problems encountered, or of the unusual instances that represent integral parts of an analytic review. With this premise in mind, we are presenting herewith several illustrative problems of comparative rarity, encountered on the Gynecological Service of Prof. Brooke M. Anspach at Jefferson Medical College Hospital.

### 1. CANCER ASSOCIATED WITH UTERINE PROLAPSE

Several comprehensive articles relating to the infrequent association of cervical carcinoma and procidentia have recently appeared.

Guthrie and Bache<sup>1</sup> in reporting a case presented a survey of the subject based upon information received by them through a questionnaire and upon a review of the literature. Their careful résumé emphasizes the rarity of these associated lesions, for it revealed the occurrence of less than 40 cases collected from the literature and from the combined experience of 48 American gynecologists and general surgeons. This paucity of reported cases, based on the observation of thousands of cases of procidentia, exhibits an exceedingly low incidence and would probably indicate an equally low incidence were it possible to consider those cases that have undoubtedly existed but have never been recorded.

Delvaux<sup>2</sup> conducted a similar review and questionnaire in France, which reveals an even lower frequency.

Högler<sup>3</sup> reviewing the records of 11,045 admissions to the Second University Woman's Clinic in Vienna, from 1926 to 1931 inclusive, noted 5 cases of prolapse among 395 patients with cervical cancer, an incidence of 1.26 per cent; while among 10,650 patients without prolapse, there were 776 afflicted with carcinoma, an incidence of 7.2 per cent.

Specific reference in the literature to fundal carcinoma associated with procidentia is lacking; probably numerous unreported instances have occurred. Guthrie and Bache mention 2 cases while McGlinn,<sup>4</sup> in 1927 reported a case that was discovered two and one-half years after the performance of an interposition operation. In discussing the latter's paper, Bissel reported 3 cases, 2 of which occurred three or more years after interposition operations while in the third case, routine study of the curettings revealed the diagnosis immediately following such an operation.

\*Read at a meeting of the Obstetrical Society of Philadelphia, Dec. 7, 1933.

On the Gynecologic Service at Jefferson Medical College Hospital, from Sept. 1, 1921, to Sept. 1, 1933, 3 cases of malignancy associated with uterine prolapse have come under our observation; 1 squamous cell carcinoma of the cervix, and 2 adenocarcinomas of the fundus. Abstracts from the case histories are herewith presented.

CASE 1.—E. E. H., aged fifty-six years, was admitted on Jan. 27, 1933, complaining of loss of perineal support, a bearing-down sensation, watery discharge, and a mass between the thighs. Married at thirty-six, her first and only pregnancy resulted one year later in a difficult forceps delivery. A year after the birth of the child, the patient experienced a sudden loss of support, and since then the entire uterus had remained outside of the vulva, but for a long time the patient herself could replace it. Following the menopause twelve years ago, ulceration had been present, and one year ago a severe hemorrhage had occurred. Since then irregular bleeding and a constantly irritating discharge, contributed to by an incontinent bladder, had been present. She also complained of a swelling in the right groin.

The patient was poorly nourished and emaciated. Protruding from the vaginal orifice was an elongated, thickened, edematous mass of tissue with a granulating surface, interspersed with areas of necrosis. The organ had been prolapsed and traumatized over a long period of time, decubitus ulceration had resulted, and it could not be replaced within the vaginal orifice. A reducible right inguinal hernia was present. Laboratory studies showed a marked secondary anemia, an albuminous urine, negative Wassermann and Kahn reaction while a dark-field examination of the lesion was negative for the *Spirocheta pallida*. Biopsy revealed squamous cell carcinoma, intermediate grade, with a marked inflammatory reaction and areas of excessive keratinization. X-ray therapy together with local palliative measures was instituted, and in a few weeks the uterus regressed within the vaginal introitus. After a course of x-ray therapy, the patient was removed to her home, where she died, April 1, 1933.

CASE 2.—M. M., widowed, aged sixty-four years, was admitted Oct. 23, 1932, complaining of a protrusion from the vagina, vaginal bleeding, and pain in the left side. Married at twenty-seven, para iv, the menopause had occurred at forty-six. The vaginal protrusion had been present for more than twenty years, the irregular bleeding for one year. Examination revealed a prolapsed, slightly irregular uterus with an intact, hypertrophied cervix, from the canal of which a slight bloody discharge was issuing. A large cystocele and rectocele were present but the adnexa were not distinguishable. Obesity, diabetes, hypertension and cardiorenal changes were present, but because of the constant local discomfort and the suspicion of uterine malignancy, vaginal hysterectomy under spinal anesthesia was performed, first closing the cervix with sutures and not curetting the uterine cavity. The Mayo technic was followed, and since the ovaries were small and atrophic, the adnexa were allowed to remain as a further aid in the correction of the cystocele, anterior and posterior colporrhaphy completing the operation. Examination of the removed uterus showed an advanced adenocarcinomatous growth invading the myometrium; also several intramural fibromyomas. Postoperative convalescence was uninterrupted. Within the past year a mass was discovered in the lower right pelvis, and a complete course of deep x-ray therapy has been employed with marked regression of the growth.

CASE 3.—P. S., married, aged fifty years, was admitted on Oct. 8, 1927, complaining of malaise, bearing-down sensations, and a protrusion from the vagina. Married at seventeen, para vi, she had menstruated regularly until a year prior to admission.

Since then the periods had been recurring from every four to eight weeks. An umbilical hernia had been operated upon nineteen years before. Marked obesity was present, but the general physical condition was satisfactory. Curettage, trachelectomy, anterior and posterior colporrhaphy, together with extraperitoneal fixation of the fundus were performed. Examination of the curettings revealed marked hyperplasia of the endometrium, probably undergoing malignant change. Postoperative convalescence was uneventful, but since adenocarcinoma was strongly suggested by the curettings, she was readmitted to the hospital on Dec. 9, 1927, the curettage was repeated, and an application of 3,600 mg. hr. of radium (three 50 mg. capsules, screened in silver, brass, and black rubber, arranged in tandem) was made to the uterine cavity. This curettage revealed very definite adenocarcinoma of the fundus and complete abdominal hysterectomy with bilateral salpingo-oophorectomy was performed some time later. The operation was technically difficult because of the extraperitoneal fixation and because of adhesions resulting from the former umbilical herniorrhaphy. The uterus when removed showed complete destruction of the endometrium, which was replaced by granulation tissue; also chronic metritis, and fibromyomata uteri. No evidence of carcinoma could be found in the structures removed. The patient has remained symptom-free, and at present is in good general health.

#### COMMENT

If chronic irritation alone be deemed essential to the development of cervical cancer, it would seem that the prolapsed uterus, exposed as it is to constant trauma, should furnish an ideal site for its inception. The rarity of these associated lesions furnishes an adequate argument against such an hypothesis, and provokes thoughtful consideration of the reason for this infrequency. One theory advanced is that free drainage from the prolapsed organ removes the constant presence of irritating secretion, indicating that an acid discharge may be a predisposing factor, and not chronic irritation alone. Another thought is that resulting cornification is protective in character, but some regard this change as precancerous (Martzloff<sup>3</sup>). Hereditary predisposition should be considered, and Masson<sup>4</sup> has pointed out that age is an important consideration. His reason is that the majority of women develop cancer at or near the menopause, at which time prolapse is not as likely to be present. Later on when prolapse may occur as a result of atrophic changes, cancer, should it develop, occurs therefore at a much later age. The presence of carcinoma in the nulliparous cervix likewise contraindicates chronic irritation as a sole cause. In the first case herewith presented the patient was married comparatively late in life, the labor was difficult, and the prolapse occurred a year later, eight years prior to the menopause, existed for eighteen years, and indicating that the carcinoma had developed after many years of chronic irritation. These observations point to the presence of a biochemical factor in the initiation of malignant change; chronic irritation alone does not seem to be a sufficient reason.

In the case of fundal cancer developing in the prolapsed uterus, the occurrence might well be coincidental. It is well known that

corporal adenocarcinomas usually develop after the menopause, paralleling in time the usual appearance of procidentia. The theory of chronic irritation is less tenable here than in cervical cancer, further substantiating the thought that there are other predisposing factors, since the development of the condition is irrespective of parity. The concomitant presence of fibromyomas has been regarded for a long time as a probable etiologic factor, but a distinct influence has been ascribed to deficient endometrial drainage (Graves<sup>7</sup>), which might be contributed to by the presence of myomas or by an atrophic, atretic cervical canal (Healy<sup>8</sup>). In both of the cases presented here, fibromyomas were accompanying lesions. Of additional interest is the manner in which the activity of the radium had destroyed all evidence of endometrial carcinoma, as disclosed by the histologic study of the removed uterus.

## 2. CERVICAL CANCER ASSOCIATED WITH PELVIC INFLAMMATORY DISEASE

We have been unable to find any specific comment in the literature relative to the occurrence of inflammatory adnexal disease and cervical cancer as distinct clinical entities.

Ruge<sup>9</sup> and others have shown that the carcinomatous cervix harbors various strains of streptococci as well as less virulent organisms, and one can readily comprehend associated broad ligament cellulitis, adnexitis, and peritonitis arising from the activity of certain lethal organisms in a manner similar to that which occurs in the postabortal or puerperal state. This knowledge has been utilized by Ruge, and in a modified form by Philipp,<sup>9</sup> in the development of the so-called "virulence test." Further evidence of the predisposition to pelvic inflammation by the infectious carcinomatous cervix is furnished by numerous reported instances in which the application of radium or the x-ray has apparently caused death either by promoting peritonitis directly or by the supposed activation of quiescent adnexal lesions. Similar untoward results have been observed following the irradiation of benign lesions.

Pickhan,<sup>10</sup> in discussing a number of irradiated cases (principally carcinomatous ones) that terminated fatally, summarizes the possible etiologic factors advanced by a group of German clinicians, including Döderlein, Lubarsch, and others. Opinions were expressed that secondary bacterial invasion of the pelvic lymphatics may originate in necrotic degenerative areas that have replaced the carcinomatous growth following a local radium application; or that instrumentation may mechanically extend a superficial infection to the deeper structures. Since infiltrating, inflammatory tissue cells are especially susceptible to irradiation, as is granulation tissue, the application of a large dose leads to rapid degeneration, liquefaction, and destruction of the inflammatory barrier. If the location of the lesion does not permit of free drainage, dissemination of the inflammatory process may readily result in fatal peritonitis. Were it possible to institute surgical drainage, the process in itself might be desirable.

No case has come to our attention, however, in which the symptoms and signs of pelvic inflammatory disease were so pronounced that cancer of the cervix, either as a primary lesion or as a coincidental



one, was overlooked. Two cases occurring on the Gynecologic Service at Jefferson Medical College Hospital presented such a problem, and, although the presentation of them emphasizes certain errors of omission, we feel that they are of sufficient importance to be abstracted briefly. A third case, representative of a primary radium mortality, is presented because of the illuminating autopsy findings.

CASE 1.—A. G., thirty-four years old, married eighteen years, para ii, was admitted on Dec. 22, 1930, because of severe bilateral abdominal pain, nausea, and chills of about a week's duration, coincidental with the expected menstrual period, which was present on admission. No prior menstrual irregularity had existed; there were no previous operations. Frequency and burning of urination accompanied the attack, the temperature was septic in type, rising daily to 101° or 102° F., with the pulse rate in proportion. A moderate anemia was present and a leucocytosis of 17,500; Wassermann, negative. Since the patient was extremely ill and vaginal bleeding was present, the cervix was not inspected in the routine manner, but by a bimanual examination made in bed. This revealed a multiparous introitus and an elongated, irregular cervix. The fundus was not well defined, being incorporated with an exudative mass occupying the entire pelvis, the adnexa being indistinguishable. On the basis of these findings, together with the history and mode of life of the patient, a diagnosis of "frozen pelvis," probably of neisserian origin, was made and expectant treatment instituted. She insisted upon leaving the hospital four weeks later, with slight symptomatic improvement and little change on bimanual examination.

The patient was readmitted on Jan. 26, 1931, because of continuance of the symptoms. The cervix was not inspected, bimanual examination revealing fixation of the uterus accompanied by a pelvic mass. Expectant treatment was again instituted, and following symptomatic improvement and regression of the pelvic mass, it was thought that operative measures could be undertaken. Routine inspection now resulted in the discovery of a friable area in the hard indurated cervix. Tissue scrapings were not conclusive of malignancy, but under anesthesia the canal was found to be obliterated by a malignant growth, biopsy of which revealed squamous cell carcinoma, well differentiated (intermediate grade). Deep x-ray therapy was immediately instituted (March 17, 1931) and continued over a period of three weeks without any reaction of consequence. Following observation in the Follow-up Clinic, 2,400 mg. hr. of radium were applied Oct. 30, 1931; hemorrhages and pain caused readmission to the hospital on Nov. 27, 1931, but no further treatment was administered. The patient then entered the Philadelphia General Hospital on Dec. 27, 1931, dying of a blood stream infection (*B. coli*) on Dec. 31, 1931. Autopsy showed myocardial degeneration; pyelonephritis with abscess formation in right kidney; no definite evidence of tumor of the pelvic organs, but marked ulceration of the body of the uterus and cervix, with fibrosis. Unfortunately a detailed report of the adnexal findings was not recorded.

CASE 2.—V. S., twenty-six years old, married nine years, para ii, was admitted on Aug. 20, 1931, because of profuse vaginal bleeding of ten days' duration, appearing one week after a delayed period, accompanied by cramplike pain in the lower left quadrant, nausea, vomiting, and abdominal distention. The menstrual history had been regular with two exceptions—periods of bleeding of two weeks' duration on two occasions during the past year. Five days after the onset of the bleeding,

pelvic pain became the prominent symptom. The temperature, pulse, and respirations were elevated moderately; the blood pressure was 122/68; Hg., 35; R.B.C., 2,690,000; W.B.C., 12,500; color index, 63; Wassermann, plus 4. The patient was very ill and examination was conducted in bed. The abdomen was markedly distended, tender, but not rigid. Dullness in the flanks suggested free fluid. Bimanual examination revealed a multiparous outlet with moderate relaxation; an indurated cervix (not inspected); uterus slightly enlarged, retroverted and fixed with bilateral tenderness in the adnexal regions. A tentative diagnosis of an infected ectopic gestation and pelvic peritonitis was made, with the possibility of the condition being entirely of an inflammatory nature. On two successive days, without undue vaginal bleeding, the blood count decreased to: Hg., 25; R.B.C., 1,500,000; W.B.C., 16,700; C. I., 0.83; with increased pulse, respiration, abdominal distention, and vomiting. Efforts were made to secure a donor for transfusion, while symptomatic and supportive treatment was continued. Pelvic examination now showed a tender exudate in the pouch of Douglas with shifting dullness. The distention continued, but the nausea and vomiting subsided. Transfusions improved the patient's general condition, the fever subsiding gradually. On Oct. 10, 1931, pelvic pain and tenderness, together with the exudative process, had subsided. The cervix was then visualized for the first time, and an indurated friable area observed suggesting a carcinomatous or syphilitic lesion. Biopsy revealed squamous cell carcinoma (intermediate grade) with a marked inflammatory reaction. Foreign protein injections begun ten days earlier were continued, as well as injections of a mixed vaccine, and the temperature reached normal and remained so for two weeks. On Nov. 13, 1931, 3,300 mg. hr. of radium were administered, followed by mild abdominal pain and irregular fever. Patient was discharged one week later. Follow-up visits showed discouraging advance of the disease with much local ulceration and discharge, the patient dying elsewhere in August, 1932. No autopsy.

CASE 3.—B. S., aged forty-eight years, married twice, para i, was admitted on Nov. 8, 1930, because of pelvic pain and postmenopausal bleeding of two years' duration. Examination revealed a carcinoma of the cervix (Class 3) with moderate pericervical induration, the fundus being fairly movable. Biopsy was conclusive of squamous cell carcinoma (low grade), and on Nov. 13, 1930, 3,600 mg. hr. of radium were administered. Within five days severe abdominal pain occurred, accompanied by chills, fever, and abdominal distention. Rapidly developing peritonitis set in with death on Nov. 20, 1930. The autopsy findings were significant. Generalized purulent peritonitis was present, cultures yielding *Streptococcus nonhemolyticus*, *Staphylococcus albus*, and *B. coli communis*. The omentum was adherent in the pelvis. The uterus was somewhat enlarged and adherent to the surrounding structures. At the base of the uterus on both the anterior and posterior surfaces, there were a few injected vessels, but no evidence of definite necrosis or perforation of the uterine wall could be demonstrated. On section the myometrium was somewhat thickened, and the uterine cavity contained a small amount of necrotic material. There was extensive necrosis of the cervix and the lower end of the fundus, involving practically the entire wall. Both tubes were enlarged, thickened, the left ovary being adherent to the tube forming a large cystic necrotic mass which contained purulent material. The right ovary appeared to be normal. While there were many adhesions to the cervix, there was no evidence of infiltration of the surrounding structures by carcinomatous tissue. The retroperitoneal lymph nodes in the lumbar region were enlarged and softened, but microscopically showed no evidence of tumor metastasis. Histologic studies confirmed the gross pathology.

## COMMENT

In reviewing Cases 1 and 2, two clinical facts are evident. First, a pelvic examination is not complete without actual inspection of the cervix, for such an error of omission may result in the overlooking of a grave lesion. Second, a fulminating pelvic inflammation may be the initial symptom-complex in cervical cancer and be the urgent factor that compels the patient to seek medical aid. It cannot be proved in the cases presented whether the pelvic peritonitis was secondary to an infected carcinomatous cervix or whether the lesions were concomitant ones of gonorrheal or mixed infectious origin. We may only surmise. Patients with pelvic inflammatory disease, of either gonorrheal or post-abortion origin, are frequently seen, in whom the presence of pelvic peritonitis is so obvious that more than a cursory initial examination is not justifiable. In a case of this type—the so-called “frozen pelvis”—thorough inspection of the introitus and especially the cervix should not be delayed after the patient's initial discomfort has subsided. In all fairness, however, these patients did not suffer because of the delayed diagnosis, for irradiation therapy could not have been instituted any earlier, and the prognosis was discouraging in both instances.

The third case emphasizes that fortunate rarity in the irradiation therapy of cervical cancer—primary mortality. The autopsy, in addition to the generalized purulent peritonitis present, revealed chronic suppurative salpingitis with abscess formation in one ovary. The supposition in this instance was that quiescent adnexal disease had existed for a comparatively long time but had not been recognized, irradiation activating the lesion.

The radium applications in these cases consisted of 50 mg. of radium sulphate sealed in glass within a silver capsule 0.3 mm. thick in turn enclosed within a brass capsule 1.0 mm. thick with further screening by black rubber tubing 2.0 mm. in thickness placed in the cervical canal. Eight needles, each containing 12.5 mg. of radium sulphate, screened by 0.3 mm. of Monel metal, were placed about the periphery of the growth.

The incidence of primary mortality following irradiation may be influenced by the extent of the lesion treated, but instances have been reported in which peritonitis and death have followed radium applications in less advanced conditions, not as a result of faulty technic, but because of the presence of virulent organisms in the cervix, the irradiated tissues, or in quiescent adnexal lesions. While it behooves us to be alert to the possible sequelae of irradiation and to observe carefully the contraindications to its use, it is truly remarkable that untoward results do not occur more frequently. Perhaps the routine employment of the virulence test would be a wise precaution prior to irradiation of the carcinomatous uterus.

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255 SOUTH SEVENTEENTH STREET

## DISCUSSION

DR. ROBERT A. KIMBROUGH, JR.—In 753 cases of cervical carcinoma at the University Hospital, only one has been seen in association with complete descensus. The lesion was so early that the diagnosis was made only on routine microscopic study of the amputated cervix. Although the prolapsus had existed for only three years, there was a rather large decubitus ulcer near the external os.

Since both procidentia and carcinoma of the uterine fundus are relatively frequent and are characteristically conditions of postmenopausal years, it seems logical to assume that their occurrence in the same individual is most likely coincidental. On the other hand, hypertrophy and edema of the cervix in many cases of procidentia may lead to narrowing of the canal, thus causing retention of endometrial secretion. If such retention, as suggested by Graves, Curtis, and Healy, favors the development of fundal cancer, procidentia may be indirectly partially responsible for the growth.

We feel that the risk can be materially lessened in the obviously infected cases by the use of deep x-ray therapy prior to the local application of radium. This applies with particular emphasis to extensive Stage III and IV cases in which the danger of infection is greater.

The cited case of cervical carcinoma complicated by pyosalpinx presents a difficult problem. The same difficulty arises in the presence of a large myoma, or particularly a degenerating myoma, complicating cervical malignancy. The advisability of radical operation, or supravaginal hysterectomy with removal of the adnexa, must be taken under consideration as a preliminary to irradiation therapy. The danger of dissemination is undeniable, but with heavy filtration and the application of radium at least 1 cm. from the surface to be treated, the danger of intestinal injury is greatly reduced. Despite the dangers inherent in this method of treatment, we feel that the ultimate risk is less than that of exposing an inflammatory mass or a degenerating tumor to intensive irradiation.

DR. JOHN MCGLINN.—I think that the association of prolapse and carcinoma is interesting, but there is no relationship. Moreover, I do not believe that chronic irritation and ulceration of the cervix plays any part in the production of carcinoma of the cervix. If chronic irritation is the cause of carcinoma, why are those parts of the body most subjected to irritation practically free from carcinoma? Eliminate carcinoma of the breast, of the cervix, and of the stomach, and you have practically no carcinomas left. They take up over 90 per cent of carcinomas of the female.

I think we are wasting time in teaching prevention by repair. What we should do is teach prevention by routine early examination, by biopsy, etc., and not by later trying to treat ulceration and erosion.

## ENDOMETRIOSIS IN LAPAROTOMY SCARS\*

EDWARD A. SCHUMANN, M.D., AND WILLIAM E. PARKE, M.D.,  
PHILADELPHIA, PA.

**O**PPORTUNITY for study of the bizarre phenomenon of abdominal scar endometrioses has been recently offered to the writers by the simultaneous admission of two women presenting this lesion, to the service at the Kensington Hospital for Women.

While the subject has several times been reviewed in recent literature, the mode of implantation of the ectopic endometrioses and certain phases of its hyperplasia in the new habitat remain as controversial questions.

Almost all of the reported cases follow a cesarean section or pelvic laparotomy, though several have followed an appendectomy.

The endometriomas usually present themselves as fairly firm nodular masses rarely larger than 3 or 4 cm. in diameter, lying in the laparotomy scar and sometimes enlarge and even discharge blood at the menstrual period. They may or may not produce localized pain, are usually attached to the sheath of the rectus muscle, and rarely penetrate the parietal peritoneum. The writers have found no report of malignancy developing in an abdominal endometrioma. Keene and Kimbrough state that such formations are restricted to the lower half of the abdomen, no case having been reported as occurring above the level of the umbilicus. This may be due to the fact that in abdominal sections where the pelvic organs are the objects of attack, the incision generally occupies only the lower portion of the abdominal wall and not to any peculiarity of the growth. This would seem to be true since German (q.v.) reports a case in which three years after cesarean section, there were noted two nodules in the scar, one above the umbilicus, in the scar itself, and one below and to the left as if it had appeared in a stitch hole. On excision both nodules proved to be endometriomas which were attached to the uterine wall, penetrating the parietal peritoneum.

CASE 1.—Mrs. J. W., aged forty-two, admitted Jan. 12, 1933, giving a history of having had the left tube and ovary removed eighteen years before. She complained of a tumor at the lower end of the abdominal scar. For two years after the operation a lump appeared at this site each month, which opened and bled at the time of menstruation. After corsets were discarded, the lump did not open, but enlarged

\*Read at meeting of the Obstetrical Society of Philadelphia, December 7, 1933.



very slowly without any periodical manifestations or discomfort. Her menstrual history was normal and physical examination showed nothing of note except locally.

A left rectus scar was found somewhat puckered at the lower end, and immediately to the left of the lower end was a cystic tumor about the size of a small hen's egg which was fluctuant and seemed to contain clear transparent fluid. The epidermis was very thin over the tumor (Fig. 1).

Pelvic examination was negative except for the absence of the left tube and ovary. No adhesions were detected. At operation the cyst did not extend into the



Fig. 1.

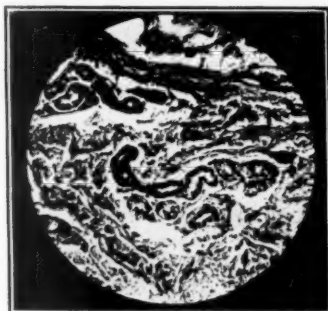


Fig. 2.

Fig. 1.—Endometriosis of the abdominal wall following left salpingo-oophorectomy, eighteen years previously (Case 1).

Fig. 2.—Low power section of Case 1 showing decided endometrial structure.

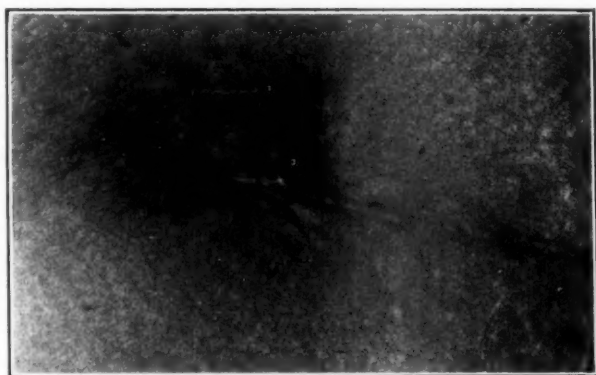


Fig. 3.—Endometriosis of the abdominal wall following active cesarean section two years previously (Case 2).

fascia, and was excised. Pathologic examination showed the presence of a thin-walled cyst lined with glands resembling endometrial glands, the epithelium of which was not well preserved and gave the impression that the glands were not functioning.

CASE 2.—Mrs. S. B., aged twenty-two, was admitted Jan. 22, 1933, giving a history of having had an elective cesarean section two years previously. The patient complained of a lump at the upper end of the abdominal scar which enlarged and became gradually more painful ten days before menstruation, during the period, and with subsidence in the ten days following. The most painful stage was during the two

days after the end of the period. Occasionally the tumor opened spontaneously and occasionally it was opened by her physician. The pain in the scar had been associated with throbbing pains in the right lower quadrant in the past three months.

Physical examination was negative except locally. There was a midline scar extending from the symphysis to the umbilicus. At the upper end just below the umbilicus was a small bluish colored mass about the size of a large pea, showing signs of having been recently opened (Fig. 3).

Pelvic examination showed the uterus normal in size but drawn high up against the abdominal wall as if a ventral suspension had been performed. Both ovaries were slightly tender. The scar was excised, and the tumor was dissected free and was found to be continuous with a thick band of scar tissue which extended to the anterior surface of the uterine fundus. Other small less dense adhesions were found and freed.

Microscopic examination of the cyst showed it to be lined with well-developed uterine glands. There was no sinus between the uterus and the cyst.

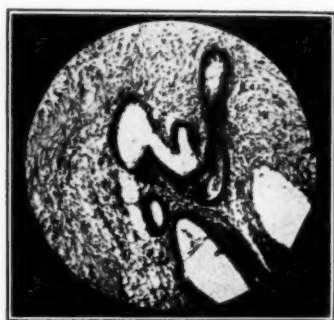


Fig. 4.

Fig. 4.—Low power section of Case 2, showing glandular structure.



Fig. 5.

Fig. 5.—High power section of Case 2, showing a typical uterine gland.

The question as to the mechanism of endometrium transplantation is still *sub judice*, but the writers believe that Sampson's theory of direct implantation, either as a result of the carrying of endometrium from a uterine incision, as in hysterotomy, to the abdominal wall, or the subsequent escape through needle punctures as in ventrofixation, is the correct one.

In support of this viewpoint, it is clear that the conditions observed in the above two cases are not compatible with any of the other theories advanced in explanation of this phenomenon.

These theories in brief may be stated as follows:

1. The wolffian theory of Von Recklinghausen who attributed endometriosis to adult remains of the wolffian system and considered these tumors organized growths in which the various structures of the mesonephron could be traced. Obviously such theory cannot be applied to postoperative occurrence of endometrium in the laparotomy scar.

2. The mucosal invasion theory of Cullen, which considers the development of adenomyoma of the uterus due to the direct invasion of the myometrium by uterine mucosa. Cullen made no attempts to explain abdominal wall endometromata on this basis.

3. The müllerian rest theory seeks to ascribe all teratomatous growths to inclusion of rests arising from adherent structures.

4. The serosal theory holds that, stimulated by inflammatory process the endothelial cells of the peritoneum may be transformed into cuboidal or columnar cells. It has also been shown that the connective tissues immediately surrounding such peritoneal inclusions may undergo hyperplasia which closely resembles the cytogenic stroma of the uterine mucosa.

This latter, which has many exponents, is obviously inapplicable to the type of case under consideration, since no explanation can be offered for the physiologic cyclical menstrual changes occurring in a true endometrium. It is, therefore, proper to conclude that the mechanical implantation of Sampson is the only explicable reason for the appearance of these abdominal implants.

Two important points remain to be cleared up by subsequent experimental work. First: it is known that many of the reported cases have followed cesarean section at term, and therefore, the implanted fragments must have been mature decidua. Now since the decidua at term is a degenerated tissue, which, when in its usual situation within the uterine cavity is entirely exfoliated and discharged during the puerperal involution of the uterus, how do these bits of nonviable cells manage to regenerate in this extrauterine location?

It has been demonstrated repeatedly that during menstruation all of the basalis and most of the spongiosa of the endometrium are cast off and that regeneration of this structure takes place from the stumps of the uterine glands which are attached to and in places penetrate the muscularis. It is difficult for a clinician to conceive of the detachment of these gland stumps in the cesarean incision and their implantation into the abdominal wall. The only reasonable explanation that offers itself to us is, that union of the uterine scar is delayed or imperfect for a period long enough to allow regenerated endometrial masses to penetrate through minute interstices between the muscles and so reach the abdominal walls. It is true that Cron and Gey (*AM. J. OBST. & GYNEC.* 13: 645, 1927) were able to prove that fragments of menstruating endometrium grew and reduplicated in culture media; while these observers secured their material by removing a large amount of menstrual epithelium from the uterus with the dull curette, it is possible that they obtained some of the basalis with its gland stumps which would explain the growth. In any case, all of these experiments have been made by using the endometrium not the senile, degenerating, mature decidua.

The second point of interest lies in the time interval between the presumable implantation and the appearance of a mass, or the development of symptoms.

The histories of 32 cases in the literature and our two have been studied with regard to this time factor which was mentioned in 19 of

the reports. In 3 "lumps" or symptoms developed in less than one year, in 6 in one or two years, and in 9 after two years, the longest interval being nine years.

Since the endometrium grows so rapidly and regenerates so quickly, this long latent period must be explained, either by some alteration in the structure of the transplanted epithelial cells, or in the time required to secure adequate vascularization in the new locality.

1814 SPRUCE STREET

1534 NORTH FIFTEENTH STREET

#### DISCUSSION

DR. FLOYD E. KEENE.—Out of more than 17,000 specimens which have passed through the University Hospital laboratory, only two adenomas are recorded. Five cases of menstruating sinuses in laparotomy scars have come under my observation and in only two of these were adenomas present, one of these following a cesarean section and the other a myomectomy and ventrofixation. In the other three patients, the bleeding occurred from a fistula which extended to the uterus or fallopian tube and in two, the fistula formation followed cesarean section. I include fistulas with the adenomatous sinuses in order to emphasize the importance of differentiating the two conditions; for obvious reasons, the operative treatment of the one would be entirely inappropriate for the other. As a means of differentiation, I would suggest a roentgenogram after injecting the sinus tract or the uterus with lipiodol. In one case, injection of the sinus with methylene blue at the time of operation was of value in tracing the fistula to the uterine canal.

So far as I have been able to ascertain, no case of adenomas of the laparotomy scar following operation for endometriosis has been reported. Under such circumstances, a certain amount of spilling and wound contamination are unavoidable, hence ideal conditions are afforded for transplantation and further development of these tumors, but in a rather large experience, I have never seen an adenoma develop after operation for endometriosis. While the weight of evidence is in favor of the transplantation origin of these adenomas, no theory has been offered which explains satisfactorily all aspects of the problem.

DR. J. O. ARNOLD.—A somewhat similar case, coming under my care at the Temple University Hospital, within the past year, has enough points of difference from those described tonight, to warrant a brief report.

The patient, a para vii, because of a double mitral lesion with failing compensation, had an abdominal delivery under local anesthesia, at about the end of her eighth month. The immediate results were good, and no difficulty was experienced until the third and fourth days, when the abdomen became greatly distended with fluid, unaccompanied with pain. On the fifth day, the incision completely reopened, and a large quantity, probably several pints, of serosanguineous fluid escaped. Fluid continued to flow rather freely for several days.

On the sixth day, I resutured the wound, inserting a rubber tube to continue the drainage. At the time of resuturing, I found a most unexplainable condition. Where, at the primary operation, there had been the thin, flaccid, abdominal wall of a poorly nourished multipara, there was now such profuse proliferation of tissue throughout the wound, that the edges were at least four times their original thickness, and were so irregular, and friable, that the resuturing was difficult. Had I not known that less than a week before, there had been no evidence of abdominal pathology, I would undoubtedly have thought only of carcinoma. Sections of tissue showed rather confusing and disconcerting conditions.

Dr. Robert T. Frank, of New York, expressed the opinion that it was "definitely metastatic carcinoma of neither intestinal nor ovarian origin." I could not, of course, believe that carcinoma could possibly be transplanted and developed so rapidly. The patient's general condition soon began to show some improvement. The drainage of fluid lessened. She ate well, and her bowels were normally active. But in a few days, less than a week, we began to find a growing mass within the abdomen, a large irregular, but nonnodular, baggy mass, occupying the whole lower left abdomen, and extending over to, and behind the subinvolved uterus, so as to be easily palpated bimanually as a soft wedgelike projection down into the recto-vaginal space. The tumor did not feel or act like carcinoma. I felt that it must be endometrial proliferation. If so, x-raying of the ovaries should inhibit its growth. This treatment was carried out on four successive days, and inside of a week, improvement and diminution in the size of the growth was clearly evident. Without other treatment, the abdominal wound healed, and soon became thin and flaccid again, and the tumor mass gradually disappeared. The patient continued somewhat cachectic but ate well and had no serious complaints. In six weeks, the abdominal growth could be found only on deep palpation, and at the end of three months, vaginal examination revealed but a very small remnant of the growth in the recto-vaginal space, and the uterus and other viscera were normal in size and position. In six months, there was absolutely no evidence in the abdominal wall, or elsewhere, that a neoplasm had ever existed.

Nine months after delivery, this patient, except for her heart lesion, was in good health, having gained 46 pounds in weight.

## THE LATERAL PELVIC ROENTGENOGRAM

### AN INTERPRETATION OF ITS OBSTETRICAL VALUE

J. BAY JACOBS, M.D., F.A.C.S., WASHINGTON, D. C.

**R**OENTGEN examination of the pelvis is now recognized as a necessary diagnostic procedure affecting the management of labor, in patients having borderline, contracted, or distorted pelvis.

Much attention has been directed to the importance of observing the contour of the plane of the superior strait. My own technic<sup>1</sup> for conducting such a study, necessitates the use of my obstetric inclinometer. With the aid of this instrument the length of the true conjugate is determined with precision, as well as the inclination of the inlet. Unless the film be made parallel to the inlet, accurate roentgenographic measurements cannot be expected. The advantages of a dependable anteroposterior view have been enumerated by many authorities.

In conjunction with a study of the anteroposterior film, a lateral picture should prove very instructive.

#### TECHNIC

The patient is placed directly on her right or left side with legs extended. The ordinary x-ray table is used with a Bucky diaphragm, if it is incorporated in the table, so that it does not necessitate elevating the patient's hips. The cassette is placed in the desired position, so that the region extending from the lower lumbar



vertebrae to the ischial tuberosities shall be brought into view. The tube is centered directly over the lateral aspect of the patient at a point about midway between the upper border of the symphysis and the bottom of the spine of the last lumbar vertebrae. The distance from the target to the symphysis pubis is noted, as well as the distance from the symphysis to the film. Exposure is now made. The film is developed at this time and the length of the conjugata vera measured by the method of Roberts.<sup>2</sup> He suggests the following formula:

Length of true conjugate on film :  $x$  :: Target to film distance : Target to inlet distance.

One may avoid the use of this equation by employing a procedure similar to, but not identical with, that used in obtaining A-P views.

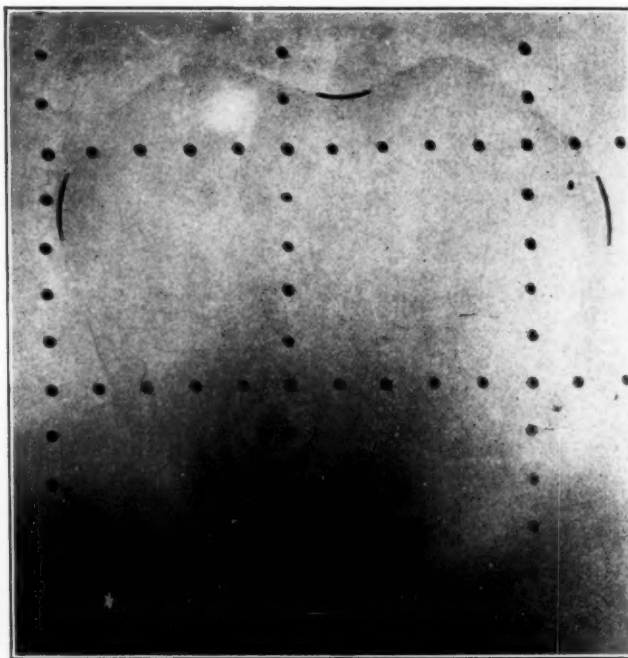


Fig. 1.—A-P Roentgenogram. This film has been subjected to 2 exposures. A picture of the inlet was taken; then the film was subjected to a second exposure, at which time the lead plate was interposed between tube and film, at level previously occupied by the inlet.

It will be recalled that in the technic employed for studying the contour of the inlet, a thin lead plate with perforations 1 cm. apart throughout its surface is utilized. This is placed between the target and film, at the station previously occupied by the inlet. The film before being developed is subjected to a second exposure, by which process shadows of the perforations are projected upon the film, so that when the latter is now developed, the transverse and anteroposterior diameters, may be read directly, by counting the dots (Fig. 1).

In the lateral roentgenograms, to avoid the mathematics suggested by Roberts, two films must be used instead of one. The first film is exposed and developed. This contains the image of the desired region. After placing the lead plate at the level of the inlet, between the target and second film, a flash exposure is made and film developed. This film will show shadows of the perforations, displaced to an extent corresponding to the distortion of the inlet on the first film. The second film

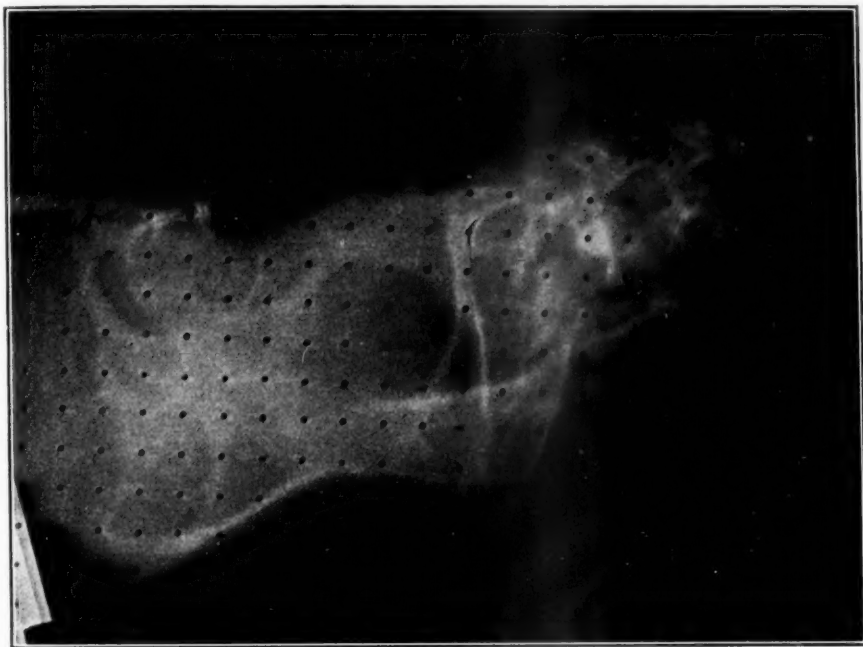


Fig. 2.—Lateral pelvic roentgenogram. Two separate films are used, each having been exposed once. The first contains the image of the pelvis, and the second which is superimposed, contains the image of the perforations in the lead plate, which had been interposed at level of inlet. Note that the second film is placed upon the first, in such a manner as to have a straight line of dots extending from the upper border of the symphysis to the promontory of the sacrum. The patient is in the recumbent posture. Inclination of the inlet is poor, and the conjugata vera measures only 9.5 cm.



Fig. 3.—Instead of superimposing the films as in Fig. 2, one may take a strip of the second film and place it on the first, in the line of the true conjugate.

White line denotes middle of upper border of symphysis. In this case, patient is also in recumbent posture. Pelvic inclination is good and T. C. measures 10.5 cm.

is superimposed on the first in such a manner that the shadows of the perforations extend in a straight line from the middle of the upper border of the symphysis to the sacral promontory (Fig. 2). By counting the dots the true conjugate diameter is measured in centimeters. Or a strip may be cut from the film containing the dots, and this placed in the line of the conjugata vera (Fig. 3).

Merely superimposing the films so that their edges coincide will not enable an accurate determination of the conjugata vera. As previously mentioned, the distance between the shadows of the perforations represents 1 cm., and each four perforations constitute a square as shown in Fig. 4. A diagonal extending between two dots, such as the dotted line in Fig. 4, represents the hypotenuse of a right triangle, the base and altitude of which each are equivalent to 1 cm. Thus, it is seen that if the perforations were projected directly on the film containing the image of the inlet and the film then developed, or in the event that two separate films were used and they were superimposed with edges coinciding, it is hardly probable that a line of

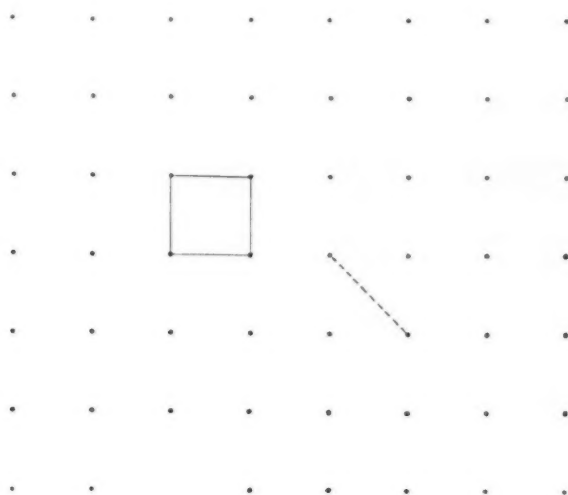


Fig. 4.—Showing that the diagonal of a square or hypotenuse of a right triangle is longer than its sides. Since the sides each represent one cm., and dotted line measures about 1.5 cm., care must be exercised in superimposing films, otherwise length of T. C. is underestimated.

dots would fall directly in the true conjugate diameter. The length of this diameter would be underestimated, since it would be composed of units, each of which may be equivalent to the hypotenuse of an equilateral right triangle.

The lateral pelvic roentgenogram possesses many points of merit. The technic is simple, and the patient is not inconvenienced in any manner.

The pictures are rather clear because some of the bulk of the fetal body and amniotic fluid which normally acts as an obstacle to penetration of the roentgen ray, is greatly avoided by this technic, as compared to anteroposterior roentgenography.

The upper border of the symphysis and the sacral promontory are brought out distinctly. In the hands of the average doctor, a picture of this type is more easily interpreted, and the mensuration of the true conjugate presents a smaller margin of error than an anteroposterior

view. I have already referred to the fact that most men are not familiar enough with this work, to accurately locate the middle of the upper border of the symphysis on an A-P film. The size of the "available conjugate," which is the distance from the sacral promontory to the most protruding portion of the upper border of the symphysis is readily measured.

The inclination of the inlet as compared to the spinal column, an important factor in the mechanical process of engagement, is readily demonstrated. As the plane of the inlet approaches the line of the spinal column, the faculty of engagement diminishes, and as it becomes perpendicular to the spinal column, the superior strait is placed in the path of the forces of expulsion, and engagement is facilitated. This is demonstrated in Fig. 5. A faulty inclination may be improved by flexing

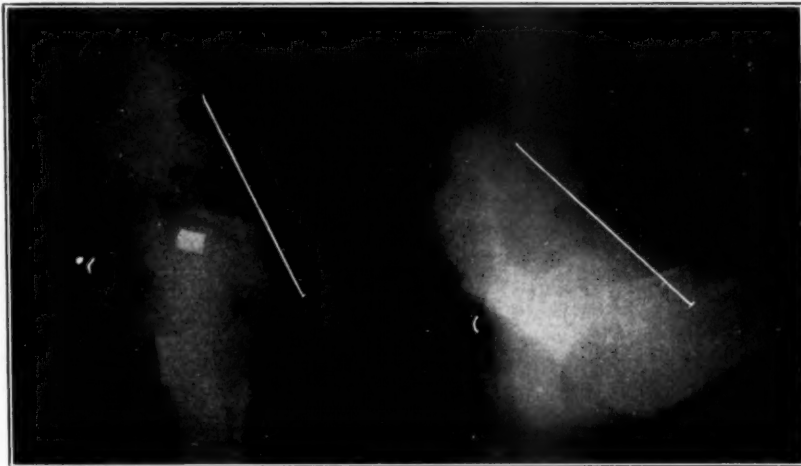


Fig. 5.—Lateral pelvic roentgenogram of patient with normal pelvis. (a) Legs extended. Note inclination of inlet and symphysis as well as size of sacrosciatic notch. (b) Thighs are sharply flexed on abdomen. Inclination of inlet and symphysis is altered. As inlet approaches perpendicular to spinal column, engagement is facilitated. By the same procedure, symphysis approaches horizontal, favoring engagement and descent. Distance from ischium to sacrum has apparently increased. Ischial tuberosity is represented in white.

the patient's thighs upon the abdomen, and thus bringing the plane of the inlet to a position that will allow the expulsive powers to drive the presenting part into the pelvis. Also by the same maneuver, a poor inclination of the symphysis pubis is corrected and may permit of engagement. This particular procedure is of great value in the management of labor in women presenting the dystocia dystrophica syndrome.

It is well to remember that failure of engagement does not necessarily signify disproportion. Inclination of the pelvic planes, especially that of symphysis and inlet, is often a governing factor, in cases where the cephalic diameters are closely adapted to the measurements of the true pelvis. In case of faulty pelvic inclination, should the pelvis be large as compared to the fetal skull, the head will have no difficulty making

a right angle turn into the pelvis. With a head and inlet of normal size, pelvic inclination may be the determining factor.

Why a roentgenologist should ever offer a prognostic prediction as to disproportion, when inspecting a flat plate picture, I am unable to understand. Even an accurate anteroposterior view in my opinion, cannot always furnish this information. For such interpretation at the present time at least, the lateral roentgenogram appears to be most promising.

The changes in the sacrum incident to rachitis, may be detected by the lateral view. The lumbar vertebrae, due to the lordosis which is common in rachitis, encroach upon the available area of the inlet and also increase the pelvic inclination. Thus, the facility of engagement is

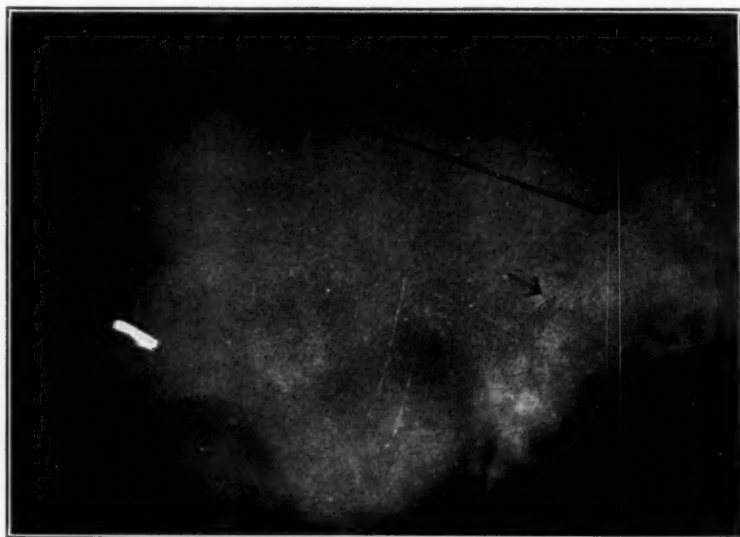


Fig. 6.—Sacrum shows evidences of rachitis. Arrow points to false promontory. Straight line indicates true conjugate diameter.

often diminished. The sacrum appears shorter from above downward and usually its vertical concavity is increased, while laterally the concavity may be obliterated or even become convex. The thickness of the sacrum from before backward is diminished, the bodies of the vertebrae protrude forward somewhat, and hence the spines do not project backward to the normal extent. Rotation of the sacrum on its transverse axis, running through the sacroiliac synchondroses, usually causes an increase in the anteroposterior diameter of the outlet. The upper portion of the anterior surface of the sacrum may be so prominent as to give the appearance of a false promontory as one encounters in the assimilation pelvis (Fig. 6). Those unskilled in pelvic mensuration, often measure the diagonal conjugate from the lower border of the symphysis to the false promontory. In this connection, I wish to stress



the importance of exploring the entire anterior surface of the sacrum, with the view of detecting evidences of rachitis, and especially the true, and the false promontory if one be present. Rarely, the distance to the false promontory is shorter than the diagonal conjugate, and for all practical purposes, warrants more consideration than the true promontory.

Reinberger and Schreier<sup>3</sup> have advocated the use of serial sagittal views to observe progress of descent during labor. This procedure, especially in borderline cases, may have practical value. The frequent application during labor, of Leopold's fourth maneuver is a safe and excellent means of gauging descent of the fetal skull, and also detecting disproportion.

Caldwell and Moloy<sup>4</sup> are calling attention to the study of pelvic architecture. This should be one of the primary considerations in any borderline or deformed pelvis. Abnormalities in symmetry, structure, and contour are observed by stereoscopic views and an attempt is made to evaluate their effect upon the mechanics involved in labor. In their lateral views, they stress the importance of the sacrosciatic notch, warning that a narrow notch brings the lateral border of the sacrum to the ischium, thus diminishing posterior pelvic capacity. This exists in the male type pelvis, which is properly designated by Caldwell, as the deep pelvis, because of the usual increase in length from above downward. A wide notch generally means ample posterior pelvic capacity. In taking lateral pictures of patients with thighs extended and then thighs flexed, for the purpose of observing the alteration in inclination of pelvic planes, I have noted an apparent lengthening in the distance between the ischium and sacrum (Fig. 5). It appears that flexing the thighs on the abdomen increases posterior pelvic capacity. My studies, however, did not include the use of the stereoscope.

I am not advocating the use of the lateral pelvic roentgenogram to the exclusion of the anteroposterior view. In a recent paper I<sup>1</sup> have described and duly emphasized the merits of anteroposterior roentgenographic pelvimetry.

#### CONCLUSIONS

1. Many points have been advanced in favor of the lateral pelvic roentgenogram.
2. A simple, accurate technic of roentgenographic pelvimetry, as applied to the lateral view is presented.
3. No technic is so simple, as to eliminate the cooperation and opinion of the obstetrician. The roentgenologist is not familiar with the use of the inclinometer, the technic of pelvic examination, and is not trained in obstetric judgment.
4. The obstetrician should be skilled in roentgenographic interpretation of the female pelvis.

5. Although the size of the pelvis is only one of many factors concerned in the mechanism of labor, it is a most important one. In the absence of an ample pelvis, successful delivery is impossible. The "practical obstetrician" who overlooks accurate pelvimetry, should not offer as his alibi, the less important factors, such as size and moldability of the fetal skull, the force and frequency of labor pains, etc.

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WASHINGTON MEDICAL BUILDING

## THE CHANGES IN THE CERVICAL MUCOUS MEMBRANE AND THE DECIDUAL REACTION IN THE CERVIX DURING PREGNANCY

HARRY B. LEVEY, M.D., KANSAS CITY, MO.

**B**EGINNING with the year 1876, much was written on the anatomy of the uterus and cervix by Bandl,<sup>3</sup> Müller,<sup>19</sup> Küstner,<sup>17</sup> Zweifel<sup>35</sup> and others. When reference, however, was made to the cervix, it appeared to involve mainly the isthmus, and very superficial and inadequate description was given of the histologic changes of the cervical mucous membrane during pregnancy. In 1877, Leopold wrote concerning the uterine mucous membrane during pregnancy and puerperium, but did not discuss the cervical epithelium. Hofmeier,<sup>14</sup> in 1886, mentions the exceedingly hypertrophied and widened glands which extend deeply into the tissue of the portio. Ballerini<sup>2</sup> and Gaifami,<sup>11</sup> in 1910, described the microscopic alterations in the portio during the various stages of pregnancy, and later, Stieve<sup>28</sup> published his splendid papers on this subject.

The material I used consisted of 12 cervixes which were taken from uteri in various stages of pregnancy, including the first, second, third, fourth, fifth, and eighth months.<sup>1</sup> Sections were made dividing the cervix into an upper, middle and lower portion, and the slides were stained with eosin-hematoxylin, mucin-carmin and the azan method.

## HISTOLOGIC DESCRIPTION

During the first month, the epithelium lining the cervical canal is thrown into many folds, which are small and occur at regular intervals. The epithelium, in general, is composed of a single layer of high columnar cells with basal nuclei. In the second month, the epithelial folds are fewer, much larger, more irregular, and

<sup>1</sup>This study was made in the I Frauenklinik of the University of Vienna. Acting Chief Dozent Dr. L. Kraul.

extend deep into the underlying tissue. Many areas of active cell multiplication are seen as shown by stratification of the epithelium with several layers of nuclei, and also, areas of double rows of epithelial cells consisting of a higher columnar layer and a lower cuboidal layer resting on the basement membrane (Fig. 1).

The glands begin to show increased activity during the first month, especially in the middle and lower portions of the cervix. The heightened response to pregnancy is evidenced by much mucin secretion, branching and infolding of the epithelium into the lumen of the glands and places where there are several layers of nuclei giving the appearance of multilayered epithelium. During the last part of the second month, the glands are wider and larger than previously. Many of them are long and tubular, simulating the corkscrew appearance of pregravid uterine body glands, and extend very deeply. New gland formations are seen as nests of large deep-staining cells. A few ciliated cells are present. Many of the glands are swollen and filled with mucin, and show a marked tendency to cystic dilatation; others are found with low columnar or cuboidal epithelium evidently denoting exhausted cells.



Fig. 1.—Photomicrograph of cervix in the third month of pregnancy, showing a double layer of epithelium.

In the third month, the epithelial projections are very marked and may assume a polypoid character. A few areas show actual downgrowth of the epithelial cells into the underlying stroma. The squamous cell epithelium does not appear to undergo any definite changes, and its junction with the columnar epithelium is clearly defined. Some sections show a thin layer of round cells imbedded in a loosened connective tissue and lying just beneath the basement membrane of the squamous epithelium. At the junction of portio and columnar epithelium, there is often seen a dense infiltration of plasma and wandering cells. According to Stieve,<sup>28</sup> these wandering cells pass through the superior layers of epithelium with resulting damage and formation of small cysts.

It is during the third month that the glands, in the middle and lower parts of the cervix, appear to have reached the height of their activity. They open widely into the cervical canal, show many atypical formations and are excreting enormous amounts of mucin. The glands extend deeply, and their fundic portion takes on finger-like projections (Fig. 4), wedge shapes, and marked branching and con-

tortion, which push downward and appear to be digging and perforating into the underlying loosened stroma. Some of the glands are surrounded by narrow streaks and bunches of muscle fibers which are remnants of the muscle tissue that has been destroyed. The thinning and swelling of the connective tissue has extended much



Fig. 2.—Photomicrograph of a section of the cervix in the fourth month of pregnancy, illustrating the lower indifferent cell layers and the overgrowing upper original columnar layer with formation of sinuses.



Fig. 3.—Shows the sinuses in the cervical epithelium of a four months' pregnancy. Many of the sinuses contain leucocytes.

more deeply. The stroma has taken on an embryonic character and is made up of large, swollen, and clear vesicular cells scattered in a delicate reticular network in which are also many plasma and round cells. Stieve has described the mucous membrane and stroma as being now, comparatively speaking, converted into a spongiosa.

In the fourth and fifth month, multilayered epithelium is more frequently found. Where this stratification occurs, one sees between the top layer of columnar epithelium and the basement membrane, a layer of indifferent cells which are very often made up of very deeply staining nuclei. These appear to be undermining and compressing the upper original columnar row of epithelium (Figs. 2 and 3). In some areas, there is a tremendous secretion of mucin with marked pressure downward on the cervical epithelium and a pressure upward by the indifferent cells, producing a flattened transitional epithelial layer. Small and large sinuses occur throughout the epithelial folds, and many of them contain polymorphonuclear leucocytes. According to Frankl,<sup>9</sup> these window-like openings are not the products of degeneration, but are due to the overgrowth and increased activity of the original superior layer of epithelium combined with the undermining influence of the indifferent cells, which leads to the formation of the sinuses.

The eighth month shows mainly, changes in the glands in the region of the internal os and the superior portion of the cervix. There is an uncommonly strong downward



Fig. 4.—Photomicrograph showing the decidual reaction in a cervix from a three months' pregnancy. Note the decidual cells extending from the basement membrane of the epithelium downward, and the round cell infiltration about them. Also the gland which sends finger-like projections, from its fundal part, downward.

growth of the glands with widening, atypical formations, and downward extension. They take on the changes that appeared in the central and lower portions of the cervix in the first three months of pregnancy.

#### DECIDUAL REACTION IN THE CERVIX DURING PREGNANCY

The decidual reaction in the cervix was described by Bayer in 1885. Beginning in 1897, cases were reported in the literature by von Franquè,<sup>10</sup> Volk,<sup>32</sup> Waldstein<sup>33</sup> and Hohmeier.<sup>15</sup> In 1905, Blumberg<sup>5</sup> described a decidual polyp taken from the cervix in a three months' pregnancy. Loeb<sup>18</sup> produced decidua in the uterus experimentally following trauma. Decidual reaction in cervical polyps was later described by Frankl,<sup>9a</sup> Taussig,<sup>30</sup> Zachonias,<sup>34</sup> Bertolini,<sup>4</sup> Hinselmann,<sup>12</sup> Stolper, Heidler, Martines, and Schereschewsky.<sup>22</sup>



Fig. 4 shows a section of the cervix from a three months' pregnancy taken just above the junction of the portio and columnar epithelium. Just beneath the basement membrane in the subepithelial connective tissue, are scattered nests of decidua cells, which extend downward.

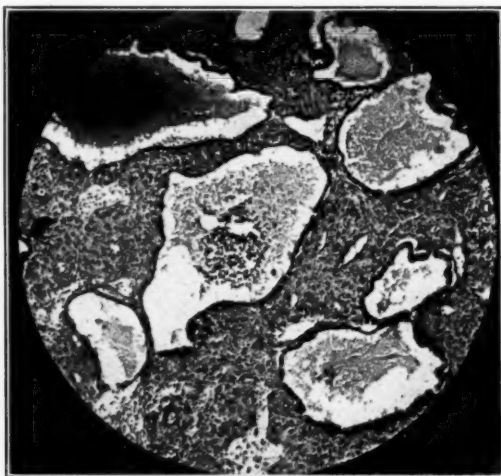


Fig. 5.—Showing intense decidual reaction in a polyp taken from a pregnant woman. Note markedly dilated glands with infiltration of round and plasma cells about the decida.

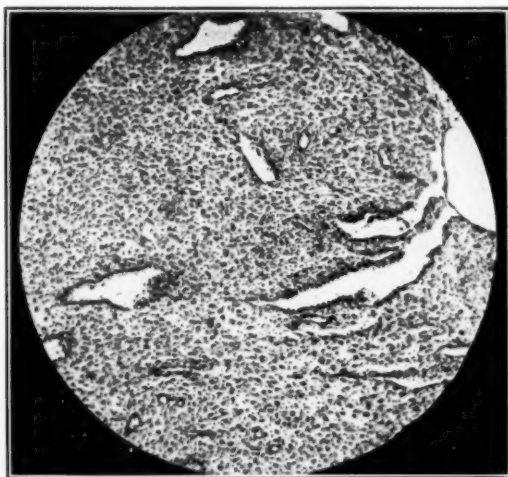


Fig. 6.—Photomicrograph of a decidua cervical polyp showing the large perfectly developed decidual cells. Note the dilated glands and the sprinkling of round cells through the stroma.

Some round cells surround the decidual nests. The reaction is very scanty and did not appear in any other sections of this cervix.

The decidual reaction was also seen in another cervix from a four months' pregnancy, and was found, as in the previous section, just above

the level of the portio. This shows perhaps a dozen typical decidual cells scattered into several small groups, and lying in the heights of the epithelial folds.

The cervical polyps, Figs. 5 and 6, were taken from pregnant women and show a marked decidual reaction which is very extensive and well developed. In association with this, one sees an intense inflammation with marked dilatation of the vessels, and many round and plasma cells scattered throughout the connective tissue.

#### COMMENT

It is generally agreed that the changes which occur in the cervical mucous membrane and glands during the various stages of pregnancy denote purely a physiologic process. It is very interesting to note that some writers have pointed out the similarity of these changes to certain pathologic conditions. In 1910, Gaifami<sup>11</sup> and Ballerini,<sup>2</sup> noted that atypical formations, which may be found in the cervical mucous membrane during pregnancy, resemble the formations found in inflammation, beginning neoplasm and even tuberculosis of the cervix. Hofbauer<sup>13</sup> believes that the cervical epithelial hyperplasia occurring in some pregnant uteri, bear some relation as an antecedent to cervical cancer, especially if these hyperplastic cervical elements persist after the termination of pregnancy. The squamous epithelium of the portio shows no definite changes during pregnancy, and no metaplasia of columnar into squamous epithelium was seen. It does not appear, therefore, that portio carcinoma bears any anlage derived from the pregnant reaction. The columnar epithelium and glands appear abnormally wild at first glance, but careful examination always reveals an intact basement membrane, mitotic figures are not often found, and the hyperplastic glands and stroma changes may well be likened to those that occur in the endometrium due to the stimulus of pregnancy.

The appearance of decidua in the cervix has been explained in many ways. Loeb believed that a traumatic stimulus was the main factor. Schoch<sup>25</sup> suggested that the decidual cells were brought down to the cervix during curettements. Meyer<sup>20</sup> maintains that the decidual ectopic nests are found mainly in the presence of local inflammatory irritation in a normal physiologic tissue which must have a certain innate pre-existing structure before decidual cells can be formed there. Frankl believes also that an inflammatory stimulus is the main factor.

The incidence of the occurrence of the decidual reaction in the cervix in pregnancy varies with different authors. Well-formed ectopic decidua cells, and not decidua-like cells, were not found as often as some authors report. Some writers give the figures as occurring in 25 per cent of their cases, others as high as 50 per cent. Tarlo,<sup>29</sup> in 1931, in an examination of 36 cervixes during pregnancy, found that diffuse decidual changes

of the cervical mucous membrane stroma were not usually noted, and reported only several collections of decidual cells. These decidual cells can be readily differentiated from the large swollen stroma cells, which are sometimes called decidua-like cells and which should not be mistaken for the true decidual cells.

#### CONCLUSIONS

1. The cervical epithelium and glands in the central and lower divisions of the cervix show their greatest activity, mucin secretion, and hyperplastic changes during the third month of pregnancy.

2. In the last few months of pregnancy, the upper part of the cervix begins to show the changes which have occurred previously in the middle and lower parts of the cervix.

3. Typical decidual cell reaction is not of relatively frequent occurrence in the cervix of pregnant women. When found, it is very scanty and ill defined.

4. The decidual reaction in cervical polyps is very much more extensive and better developed than in the cervix proper because of co-existing local inflammatory irritation.

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## A PUPILLARY SIGN IN RUPTURED ECTOPIC PREGNANCY

U. J. SALMON, M.D., C.M., NEW YORK, N. Y.

*(From the Gynecological Service of the Mount Sinai Hospital)*

**D**URING the course of the routine physical examination of a patient suspected of having a ruptured ectopic pregnancy, a unilateral dilatation of the pupil was noted. At laparotomy about a liter of fresh blood was found in the peritoneal cavity and the bleeding traced to a ruptured tubal ectopic gestation. After operation the pupils were found to be equal in size and remained so throughout the patient's convalescence. At the time of admission it was noted that the patient complained of severe right shoulder pain, and it was felt that the dilated pupil might, like the shoulder pain, be caused by the intraabdominal hemorrhage. Accordingly, during the following ten months, the pupils were carefully examined in all patients suspected of having an ectopic pregnancy. During this period 16 patients with ruptured ectopic pregnancy were operated upon, and in 4 of these, preoperatively, a unilateral dilatation of the pupil was noted, the dilatation disappearing in all cases after operation.

CASE 1.—E. G., aged thirty-six, married eight and one-half years, never gravid. Menstrual history:  $14 \times 28 \times 2$ . Last menstrual period occurred four weeks previously and consisted of spotting for one day. On the following day patient experienced midline lower abdominal pain which persisted for three days. Lower abdominal pain increased twelve hours before admission and radiated upward toward the epigastric region. Several hours before admission the pain radiated to the right shoulder and right side of the neck.

On physical examination the temperature was  $100^{\circ}$ , pulse 120, respirations 24. There was marked pallor. The right pupil measured 4 mm. in diameter, the left 2 mm. There was diffuse lower abdominal tenderness, shifting dullness, and lower abdominal spasticity. Pelvic examination revealed the cervix to be exquisitely tender to manipulation. The culdesac appeared full and distinctly tender. The uterus and adnexa could not be defined because of the tenderness. Hg. 70 per cent; sedimentation time ninety-seven minutes, blood pressure 90/58.

Laparotomy was performed and the abdomen was found filled with fresh blood. A left ruptured tubal ectopic was found and left salpingo-oophorectomy done. Immediately after operation both pupils were equal in size, measuring about 1 mm. in diameter. During convalescence, which was uneventful, the pupils remained equal in size. When seen again, four months later, both pupils were round, regular, of equal diameter. Wassermann negative.

CASE 2.—H. P., aged thirty-one, married seven years, never gravid. Menstrual history:  $12 \times 28 - 30 \times 3$ . Last menstrual period was four weeks before admission, lasting four days. One week before admission patient had an attack of lower abdominal pain lasting one hour. Pain recurred five days later, spreading from

lower abdomen upward and over the front of the chest. On the evening of admission patient had severe lower abdominal pain accompanied by right supra-scapular pain radiating down the right side of the chest. There was slight vaginal spotting on the day before admission.

On physical examination the temperature was 98° F., pulse 126, respirations 20. Marked pallor of the mucous membranes was apparent. The right pupil was dilated to 5 mm., the left to 3 mm. The abdomen was distended and there was dullness in the flanks. There was diffuse tenderness over the whole abdomen. Pelvic examination: Retroverted uterus of normal size. Exquisite pain on moving cervix. Right fornix and culdesac bulged by a cystic globular mass which was very tender. Blood pressure 70/40, Hg. 60 per cent, sedimentation time sixty-five minutes; urine examination, negative.

At operation, the abdomen was found to be filled with bright blood and old blood clots. The right tube was found to be the site of an ectopic pregnancy which had ruptured. Both tubes were thickened and bound down by adhesions. A right salpingectomy was performed. After the operation both pupils were regular and equal in size, measuring 2 mm. in diameter. During the fourteen days of her stay the pupils were equal in diameter.

The patient was seen one and three months later at the follow-up clinic and the pupils were found equal in diameter. Wassermann negative.

CASE 3.—M. M., aged twenty-nine, married thirteen years, gravid iii, para i. Menses: 12 × 30 × 3. Last menstrual period was delayed seven days and was followed by spotting four days later. Two days before admission patient experienced mild right supraclavicular pain followed by L.L.Q. pain and a sensation of pressure in the rectum. Twelve hours before admission patient experienced severe L.L.Q. pain. One hour before admission there was severe right shoulder pain, following which she fainted.

On physical examination the temperature was 99° F., pulse 106, respirations 20. Patient appeared pale. The right pupil was definitely dilated. The abdomen was distended and tender throughout, tenderness being most marked in L.L.Q. There was percussable dullness in the flanks. On pelvic examination the uterus was found to be slightly enlarged. The cervix was tender to manipulation. A soft, tender, boggy mass could be felt in the left fornix extending behind the cervix. Hg. 70 per cent, blood pressure 110/80, sedimentation time fifty minutes.

At operation the abdomen was found full of bright blood. The right tube and ovary were normal. The left tube also appeared normal but bright blood was seen trickling from the ostium. A left salpingectomy was performed. Pathologic report: tubal ectopic pregnancy.

Following the operation both pupils were pinpoint and equal in size. Throughout her stay in the hospital, of eighteen days, both pupils remained equal in size. This patient was seen in the follow-up clinic three and seven months later and on each occasion the pupils were equal. Wassermann negative.

CASE 4.—R. B., aged twenty-four, married four years, one spontaneous abortion two years ago. Menstrual history: 13 × 28 — 31 × 3 — 4. Last menstrual period eight weeks before admission. Four days before admission the patient was seized with severe L.L.Q. pain lasting several hours. Thereafter she was free of pain until fifteen hours before admission to the hospital when she experienced severe R.L.Q. pain radiating to the rectum. On admission, patient complained also of left shoulder pain.

On physical examination the temperature was 100.2° F., pulse 88, respirations 20. There was tenderness and spasticity in the R.L.Q. The right pupil was



slightly wider than the left. Pelvic examination: Uterus slightly enlarged. There was marked tenderness on manipulating the cervix. A boggy, tender mass could be felt in the right adnexal region and culdesac. Hg. 88 per cent, blood pressure 126/80, sedimentation time sixty minutes.

At laparotomy, a considerable amount of fresh blood was found in the peritoneal cavity. The right tube was the site of a ruptured ectopic pregnancy. Right salpingectomy was performed. Convalescence was uneventful. Pupils, on discharge, were equal in size. Wassermann negative.

It is interesting to note that in all of the four patients that had manifested a dilated pupil, shoulder pain was a prominent symptom. However, the dilated pupil and shoulder pain were not always on the same side. In one case the right pupil was dilated and there was left shoulder pain.

RELATIONSHIP OF DILATED PUPIL TO SHOULDER PAIN

	SHOULDER PAIN	PUPIL	ECTOPIC
Case 1	Right	Right	Left
Case 2	Right	Right	Left
Case 3	Right	Right	Right
Case 4	Left	Right	Right

In the first case observed the occurrence of the dilated pupil on the same side as the shoulder pain led to the suspicion that possibly the two phenomena were attributable to the same cause. And inasmuch as it is a generally accepted view that the shoulder pain in these cases of intra-abdominal hemorrhage is caused by irritation of the diaphragm with consequent spread of afferent impulses through the phrenic nerve to the adjacent segments of the cervical spinal cord, it was felt that the dilatation of the pupil might be caused by a similar mechanism.\*

\*Since the paper was submitted, three additional cases of unilateral dilatation of the pupil in ruptured ectopics have been observed. In one the dilatation persisted for twenty-four hours after operation.

**Mathias, Ernst: Report of an Arrhenoblastoma Removed at Operation With Subsequent Pregnancy, Zentralbl. f. Gynäk. 57: 449, 1933.**

A seventeen-year-old girl had had a period of amenorrhea of two years' duration. During this time masculine characteristics developed. These included: beard growth, rearrangement of pubic hair to the male type, loss of feminine body form, voice alteration similar to the breaking of the male voice at puberty and based on anatomical changes in the larynx, enlargement of the clitoris until it resembled an hypospadiac penis. After the two-year amenorrheic period, the menses reappeared. A solid ovarian tumor was discovered, removed and thought to be a teratoma. The tumor was found to be an arrhenoblastoma. The secondary male sex characteristics disappeared, with exception of the male type of pelvis and the voice changes, upon removal of the tumor. The patient subsequently conceived and was delivered by section because of the male type of pelvis. The author was able to find only 4 similar cases, with subsequent pregnancy, in the literature.

WILLIAM F. MENGERT.

## GRANULOMA OF THE CERVIX\*

WILLIAM B. MCGEE, M.D., NEW ORLEANS, LA.

*(From the Department of Gynecology of Louisiana State University Medical Center  
and the Charity Hospital of Louisiana, New Orleans)*

THE small series of cases of granuloma of the cervix which we are reporting in this paper is presented because of the rarity of the condition and also to stress the importance of biopsy in diagnosis. Our series consists of eight cases, similar in type, all colored patients who were sent to Charity Hospital with a tentative diagnosis of carcinoma of the cervix. Two patients died, and we lost track of one. The remaining five were followed up over a period of months. A brief report of each case is given below.

CASE 1.—A colored woman, twenty years old, was admitted on Jan. 27, 1933, with a complaint of vaginal bleeding of one month's duration, pain in the lower abdomen, weakness, and loss of weight. She had been married three years and had had one spontaneous abortion at two months. Menstruation was normal.

The pelvic examination gave the following findings: The abdomen was rigid. The cervix was rough and friable, and there was a profuse, pink vaginal discharge. Speculum examination of the cervix showed it to be composed of a firm, irregular, granular mass which bled easily on manipulation. A Wassermann test made in 1932 gave a positive reaction, and the patient had received antisyphilitic treatment.

Two different Wassermann tests in the hospital gave negative results and cervical smears were negative for Donovan bodies. The patient ran a mild spetic fever.

The report from two biopsies was nonmalignant granulation tissue.

The cervix was treated with acetone. The patient was discharged unimproved after one month and did not return to the clinic. Her family physician treated her for vaginal bleeding, weakness, and lower abdominal pain. She became progressively weaker and died on May 25, 1933. A necropsy was not performed.

CASE 2.—A colored woman, aged twenty-three years, was admitted to the hospital on Jan. 29, 1933, with complaints of postpartum bleeding over a period of three months, pain in the right side for two years, and vomiting. The menstrual history was normal. The patient had had three normal pregnancies.

Five months previous to her admission to the hospital, during her fourth pregnancy, severe pains developed in the right lower quadrant, accompanied by nausea and vomiting and continuing up to the time of delivery at full term. She was in labor for three days, and the child was delivered by forceps. A grapelike mass was found attached to the placenta. Three months later the patient was admitted to the hospital.

Pelvic examination showed that the cervix was replaced by a grapelike mass of soft, friable tissue which bled upon the slightest manipulation. The uterus was fixed. Marked tenderness was noted in the right adnexa. A large cauliflower

\*Read before the New Orleans Obstetrical and Gynecological Society, October 26, 1933.

mass was found attached to the cervix and extending to the mucous membrane of the anterior wall and the fornix of the vagina.

A tentative diagnosis of carcinoma or chorioepithelioma of the cervix was made.

The Wassermann reaction was negative and cervical smears were negative for Donovan bodies. The report from three biopsies was nonmalignant granulation tissue.

On February 14, with the patient under spinal anesthesia, the cauliflower mass was removed by actual cautery and she was given 4,800 mg. hr. of radium. A severe postoperative diarrhea developed. On March 13, the cervix was again cauterized, and after a period of one week the patient was discharged, clinically improved. After two weeks, she began to lose strength and became paralyzed from the waist down. Incontinence of feces developed and severe pain was present in the lower



Fig. 1.

Fig. 1.—Case 1. Photomicrograph showing numerous polymorphonuclear leucocytes, occasional plasma cells, and new blood vessels. (High power.)

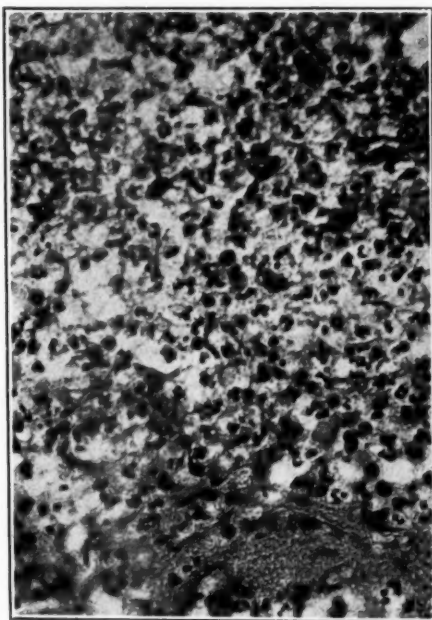


Fig. 2.

Fig. 2.—Case 2. Photomicrograph showing marked infiltration of white blood cells and many new blood vessels. (Low power.)

abdomen and the rectum. In April a rectovaginal fistula was found, and in May, a vesicovaginal fistula developed. The patient was kept under opiates during the last three weeks of life. She died June 23. A necropsy was not performed.

CASE 3.—A colored woman, sixty years old, entered the hospital Feb. 7, 1933, with complaints of pain in the lower abdomen of five years' duration, and spotting at irregular intervals. The patient had had three normal pregnancies. The menopause had occurred at the age of forty-five years.

The pelvic examination revealed an old second degree laceration of the perineum, with a first degree cystocele and rectocele. There was a profuse pink, purulent vaginal discharge. The uterus was fixed and normal in size. The broad ligament showed induration. The cervix was red and inflamed, bled on slight manipulation and was adherent to the wall of the vagina.

The Wassermann reaction was negative and cervical smears were negative for Donovan bodies.

The tentative diagnosis was carcinoma of the cervix with metastasis to the broad ligaments, and pyometra.

On Feb. 21, 1933, with the patient under spinal anesthesia, dilatation and curettage were done, disclosing a small amount of pus in the uterine cavity. The biopsy report was granuloma of the cervix.

The patient was discharged on Mar. 2, 1933, clinically improved. On June 10, and again on October 7, her family physician reported a general improvement in her condition. A few red spots were still present in the cervix.

CASE 4.—A colored woman, forty-two years old, was admitted to the hospital Mar. 8, 1933, complaining of metrorrhagia extending over a period of five years, profuse leucorrhea for two years, and a bloody vaginal discharge for one year. The patient had had three normal pregnancies. The menopause had occurred at the age of forty years.

Pelvic examination showed relaxation of the pelvic floor. The uterus was normal in size and in good position. The adnexa could not be palpated. The cervix had lost its normal contour, the anterior lip being made up of an irregular, soft, hemorrhagic mass, which bled on palpation.

A tentative diagnosis of carcinoma of the cervix was made. Three Wassermann tests were reported negative and cervical smears were negative for Donovan bodies. The report from two biopsies was granuloma of the cervix.

The patient returned to the out-patient clinic and received antisyphilitic treatment before being seen in the gynecologic clinic May 15, 1933. The condition of the cervix was unchanged at this time. Ten cubic centimeters of a 1 per cent solution of antimony and potassium tartrate were given once a week for the next eight weeks. The area of granulation tissue became progressively smaller until it completely disappeared, and the cervix returned to its normal size. The patient was discharged Oct. 5, 1933, clinically improved.

CASE 5.—A colored woman, thirty-seven years old, presented herself at the hospital, complaining of profuse leucorrhea, metrorrhagia for one month, and pain in the lower abdomen extending over a period of ten days.

The menstrual history was normal. The patient had had eight normal deliveries and three abortions.

The pelvic examination revealed a relaxed pelvic floor and vaginal bleeding. The cervix was enlarged to three times its normal size and was irregular in shape. The uterus was slightly larger than normal and was in good position. The adnexa could not be palpated. The cervix was completely covered with red granular tissue which bled freely on palpation. There was a punched-out area of ulceration about 1 cm. in diameter on the posterior lip.

The tentative diagnosis was advanced carcinoma of the cervix with metastasis.

The Wassermann reaction was weakly positive. Cervical smears were negative for Donovan bodies. The report from two biopsies was granuloma of the cervix.

The patient was discharged from the hospital on March 30, unimproved. She received antisyphilitic treatment at the out-patient clinic after which she returned to the gynecologic clinic, complaining of the original symptoms. Once every three weeks during the next four months, she received 10 c.c. of a 1 per cent solution of antimony and potassium tartrate intravenously. The cervical lesion became progressively smaller until it completely disappeared. The patient was discharged on Sept. 7, 1933, improved.

CASE 6.—A young colored woman, nineteen years old, was admitted to the hospital on Apr. 5, 1933, complaining of foul leucorrhea, pain in the lower abdomen, and a bloody vaginal discharge which had been present for one month.

The menstrual history was normal. The patient was not married and had never been pregnant.

Pelvic examination showed a marital outlet. There was a foul, watery, vaginal discharge. The cervix was firm and enlarged to twice its normal size. The uterus was normal in size and position. Tenderness was present in both adnexa. A large, friable, cauliflower mass was present involving the entire cervix. This mass bled easily on manipulation.

The tentative diagnosis was carcinoma of the cervix.

The Wassermann reaction was strongly positive. Cervical smears for Donovan bodies were negative. The biopsy report was granuloma of the cervix.

On Apr. 15, 1933, with the patient under nitrous oxide anesthesia, the cervical lesions were cauterized.

She was discharged on Apr. 20, 1933, improved, and received antisyphilitic treatment at the out-patient clinic. When she returned to the gynecologic clinic on June 8, some improvement in the condition of the cervix was noted, and no symptoms were in evidence. Antimony and potassium tartrate were administered once a week for four weeks, with marked improvement, until the lesion was reduced to a small area around the external os. This area was cauterized and three more injections of antimony and potassium tartrate were given. The patient was discharged on Oct. 5, 1933, at which time the cervix was normal.

CASE 7.—A colored woman, fifty-six years old, was admitted to the hospital complaining of backache, a yellow vaginal discharge, and progressive weakness over a period of three weeks.

The patient had had five normal deliveries. The menopause had occurred at the age of forty-one years.

Pelvic examination disclosed a senile vagina. Severe vaginitis and a purulent discharge were present. The cervix was small. The uterus was atrophic, the adnexa normal. There was a suspicious erosion around the external os which bled during the vaginal examination.

The tentative diagnosis was carcinoma of the cervix and senile vaginitis.

The Wassermann reaction was negative.

With the patient under spinal anesthesia, dilatation and curettage were performed. The biopsy report was granuloma of the cervix. The patient was discharged May 6, 1933, and could not be found for a follow-up examination.

CASE 8.—A colored woman, twenty-two years old, was admitted to the hospital May 12, 1933, complaining of foul leucorrhea, which had been present for nine months, vaginal bleeding for one month, and pain in the lower abdomen of three weeks' duration.

The menstrual history was normal.

The patient had one child, nine years old, and had had an abortion at twelve weeks, three years previous to coming to the hospital.

The pelvic examination showed slight relaxation of the pelvic floor. There was a foul, brownish vaginal discharge. The cervix was large, firm, and irregular in shape. The uterus was in good position, and was slightly larger than normal. The adnexa were indurated. A large cauliflower growth involved the entire cervix. This mass was soft and friable, and bled freely on slight manipulation. Several small punched-out ulcers were present on the anterior lip of the cervix.

The tentative diagnosis was carcinoma of the cervix.

The Wassermann reaction was strongly positive. Repeated cervical smears were negative for Donovan bodies. Report from two biopsies was granuloma of the cervix.



The patient was discharged May 25, 1933. She returned to the out-patient department for antisyphilitic treatment. At the time of her first visit to the gynecologic clinic, June 8, there was no improvement in the condition of the cervix.

After treatment with antimony and potassium tartrate, progressive improvement was observed, and the patient was discharged Oct. 12, 1933, clinically improved.

In reviewing the literature regarding granuloma of the cervix, very few articles were found describing lesions of the cervix, similar to those which were found in our cases.<sup>1, 2, 3</sup> The pathologic conditions found in our series of cases should probably be classed in the same group with granuloma inguinale<sup>4</sup> although the latter lesion involves only the skin and subcutaneous tissues. The lesions described in our cases must be differentiated from syphilis and tuberculosis.<sup>5, 6</sup> A microscopic picture very similar to that of granuloma of the cervix is presented by esthiomene, which has been described as a progressive ulceration of the vulva and vagina with elephantiasis<sup>7-15</sup> and healing fibrosis. Similar cases of granuloma involving the inguinal glands, vulva, and vagina have been reported.<sup>16-32</sup> Lymphogranuloma inguinale, a disease that involves the lymph channels and nodes, can be differentiated by the presence of the multiple small, broken-down abscesses, and by Frei's test.<sup>33-40</sup> Carcinoma and sarcoma can be definitely ruled out by microscopic examination. Other rare lesions which must be taken into consideration are yaws, leishmaniasis, rhinoscleroma, ulcus molle, blastomycosis, leprosy, and sporotrichosis, all of which have been found on the external genitals.

#### PATHOLOGY

The microscopic findings are similar in all eight cases of the series. The lesions show a marked infiltration of polymorphonuclear leucocytes, numerous new blood vessels, and a loose structure of young fibrous tissue. The most characteristic finding is the large number of inflammatory cells, nearly all being neutrophilic polymorphonuclear leucocytes, throughout the entire field. A few eosinophils and lymphocytes are found in various numbers. A very few plasma cells are present. The fibroblasts are large with light staining nuclei. In some parts of the sections the granulation tissue is replaced by fibrous tissue containing numerous mature fibrocytes and very little vascularization. A few inflammatory cells are present in the fibrous portions of the section, which appear to represent a healing stage of the process. The walls of the new blood vessels are very thin, most of them being lined with only one layer of endothelial cells. In other fields, the cells which line the newly formed capillaries form numerous buds of solid strings which resemble epithelial cells, except that they are distinctly longitudinal in shape, the nucleus is larger, and takes an even, light stain. On the borderline of the lesion, the young, vascular granulation tissue infiltrates and undermines the epithelial layer of the cervix and can be found between the cervical glands.

The epithelium of the affected parts of the mucous membrane shows a slight degree of hyperplasia with some increase in the secretion of the cells lining the glands.

#### DISCUSSION

No atypical epithelial cells which would indicate the presence of a malignant condition were found in any of the sections. The differential diagnosis must be made between a nonspecific process and syphilis or tuberculosis. The absence of necrosis, of tubercle formation, of a typical syphilitic vascular reaction, and the presence of a large number of polymorphonuclear leucocytes, speak against a specific inflammatory process. Although many polymorphonuclear leucocytes are present, the condition cannot be called a purulent or suppurative cervicitis, because of the rich development of the young granulation tissue, which indicates the chronic nature of the disease.

Antisyphilitic treatment had no effect, and cauterization resulted in very slight improvement. Although no Donovan bodies were found in the five cases in which antimony and potassium tartrate were administered, progressive improvement was noted until the lesion finally disappeared. For these reasons the condition has been classified as nonspecific granuloma of the cervix.

#### SUMMARY

The importance of biopsy as a diagnostic measure in all cases of suspicious lesions of the cervix is advocated before any form of treatment is undertaken.

The use of radium in the treatment of granuloma of the cervix is contraindicated.

Five cases responded well to treatment with antimony and potassium tartrate.

I wish to express my thanks to Dr. E. von Haam for his assistance in supplying me with the pathologic reports.

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511 MEDICAL ARTS BUILDING

## PREGNANCY IN AN ATRETIC UTERINE HORN

JOHN M. NOKES, M.D., UNIVERSITY, VA.

(From the Department of Obstetrics and Gynecology, University of Virginia)

THE following case is reported because of its interest from a diagnostic viewpoint associated as it was with an attempted induction of abortion. It is also undoubtedly an instance of transmigration of the fertilized ovum or sperm.

*Mrs. W. H. G.*—The patient, a nineteen-year-old married woman, was admitted to the hospital December 26, 1932, complaining of "death of fetus" and wishing it to be removed instantly. She was married in April, 1932, and the last menstrual period occurred on June 15, 1932.

*Present Illness.*—She considered herself normally pregnant until October 22, when she was seized by lower abdominal cramps associated with vaginal bleeding and passage of clots. Fetal movements were felt about the middle of October, but ceased on October 22. Bleeding continued from October 22 to the time of admission on December 26, although somewhat diminished in amount. The pains throughout the lower abdomen have been fairly constant since October but seem to have increased in severity during the two weeks prior to admission and at times were so severe that the weight of the bedclothes could scarcely be tolerated on the abdomen. Breast changes and morning sickness were said to have been present during August and September but had disappeared entirely since then. Seventy-two hours prior to admission nausea and vomiting recurred, associated with severe abdominal cramps. At the time of admission the patient emphatically denied any attempts to interrupt pregnancy, but several days later she finally admitted having been to a professional abortionist October 22 and again November 24. On these occasions a dilator was inserted into the cervix causing considerable pain, as no anesthetic was used. Each time the dilator was used there was an increase in the amount of vaginal bleeding.

*Past History.*—Except for an attack of cystitis when she was eleven years old, there had been no serious illnesses. Menses were regular prior to the present illness. There had been no previous operations.

*Physical Examination.*—At the time of admission to the hospital the temperature was 99° F.; pulse, 100; respirations, 30. The patient seemed acutely ill, having a haggard expression and some pallor. The general physical examination with the exception of the abdomen and pelvis was essentially normal. Abdominal examination revealed some distention of the upper abdomen with definite tenderness, spasm, and

slight rigidity. The liver, spleen and kidneys could not be palpated. There was a firm, tender, irregular mass arising above the symphysis and extending to two fingerbreadths above the umbilicus. No fetal small parts could be outlined and no fetal heart was heard. Vaginal examination showed normal external genitals with marital introitus. The cervix was large, boggy, and lacerated showing definite evidence of recent trauma. Posterior to the main abdominal mass described above there was a soft, symmetrical mass about one and one-half times the normal-sized uterus, which seemed to be connected with the cervix. Only one cervical opening could be seen. Exquisite tenderness prevented an accurate determination of the relationship of the pelvic masses. On bimanual examination it was impossible to outline the course of the round ligaments.

*Laboratory Examinations.*—Hemoglobin, 80 per cent (Dare); red blood cells, 3,720,000; white blood cells, 14,400. Smear showed slight anisocytosis. Four days after admission, examination of the blood showed hemoglobin 80 per cent (Dare);



Fig. 1.—Rudimentary horn sectioned.

red blood cells, 3,800,000; white blood cells, 11,600. Blood Wassermann was negative. Friedman test was strongly positive. Catheterized urine showed very slight trace of albumin, innumerable white blood cells with clumps, an occasional red blood cell, and no casts. An x-ray picture of the abdomen showed a small fetus, approximately six months in development.

After several days' observation with no change in the general condition of the patient, an examination under anesthesia was done. At this time the firm mass felt abdominally seemed to be definitely separated from the posterior mass in the culdesac. The latter was perhaps a little larger than the normal-sized uterus but was little if any softened. The main abdominal mass was exceedingly firm and felt more symmetrical than formerly and extended two fingerbreadths above the umbilicus. One was able to trace a band running from the anterior surface of the mass in the culdesac to the posterior wall of the firm, anterior mass. A probe passed into the cervix entered the posterior mass to the extent of its enlargement. The round ligaments could not be traced.

A tentative diagnosis of extrauterine pregnancy or rudimentary horn pregnancy was made and laparotomy advised. Five hundred cubic centimeters of citrated blood were given preoperatively.

Operation.—January 7, 1933, twelve days after admission to hospital.

Midline incision was made extending from the symphysis to the left of and just above the umbilicus. When the peritoneal cavity was opened, moderate injection of the peritoneum was noted; and a large rounded mass somewhat cystic in nature, whose surface was covered by very tortuous blood vessels, was found arising from the left cornu of the normal-sized uterus. The left tube and ovary were normal and lateral to the main mass. The uterus itself was slightly larger than normal and was to the right and in the culdesac. The tube and ovary on the right side were normal. There was marked congestion around the base of the left broad ligament, while the left round ligament was lateral to the mass described above. The

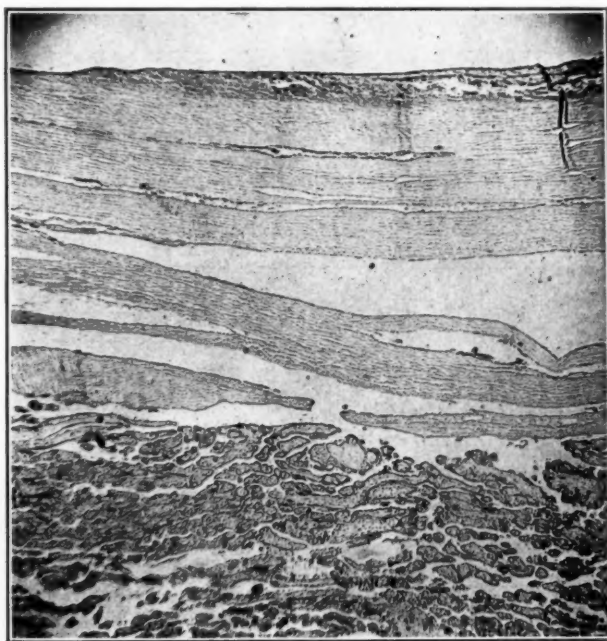


Fig. 2.—Section through the thinnest portion of the wall of the rudimentary horn.

broad and round ligaments on the left side were clamped, cut and tied, the left tube and ovary being removed with the rudimentary horn. The bladder reflection which was markedly distorted was dissected free from the main mass, which was attached to the left cornu of the uterus by a very small pedicle. The pedicle was clamped, cut and ligated. No cervical opening could be seen or probed. The pedicle seemed to be composed of large blood vessels and some fibrous tissue. The round and broad ligaments were sutured to the left cornu of the normal uterus and the bladder reflection was used to cover over the raw surfaces. The uterus itself was somewhat conical in shape. On the posterior surface of the uterus there was a weakened spot which was thought to be a partial perforation, perhaps the result of the attempted instrumentation, but while the muscle wall was weakened in one area, the peritoneal coat was intact. The upper abdomen showed evidence of recent generalized peritonitis. Only one cervix could be identified. In view of the weakened spot in the cornu of the uterus where the rudimentary horn was attached and in view of the general appearance of the uterus it was thought best



that no further pregnancies be allowed in spite of the fact that the patient was without children and was only nineteen years of age. Accordingly the right tube was cut and doubly ligated with braided silk. The appendix was not investigated. The abdomen was closed in the usual manner without drainage.

The patient bled for several days after operation, but at no time was there any decidual-like tissue passed. The postoperative course was uneventful and the patient was discharged on the fifteenth day. Subsequent follow-up examination did not reveal any menstrual irregularities.

*Pathology Report.*—Gross specimen consisted of an ovoid, semicystic mass about 15 cm.  $\times$  18 cm. The surface was bluish gray and was covered by numerous dilated and tortuous veins. At the site of amputation there were numerous blood vessels, but no opening could be identified. The left tube and left ovary were intact and showed normal relationship.

On section of gross specimen (Fig. 1) there was a laminated appearance to the wall of the horn. The placenta had a weblike appearance and covered the entire surface. The wall was thickest at the fundus and thinnest near the site of amputation. The pedicle did not reveal any opening and seemed to consist of large blood vessels and fibrous tissue. The fetus was normal in development for a six months' fetus and was not macerated. There was practically no amniotic fluid present.

Microscopic examination (Fig. 2) through a portion of the wall of the rudimentary horn (magnification 20 times) showed the wall to consist chiefly of fibrous tissue rather loosely arranged. With van Gieson's stain there was seen some muscle tissue with moderate hyalinization. The placenta was attached to the inner surface.

#### DISCUSSION

Careful study of the left ovary, removed with the rudimentary horn, failed to reveal any evidence of a corpus luteum of pregnancy. As there was no evidence of communication between the proximal end of the rudimentary horn and the uterine cavity, this was undoubtedly an instance of transmigration of the fertilized ovum or sperm. Transmigration has been noted in many of the reported cases and occurred in 78 per cent of the 84 cases collected from the literature by Kehrer in 1910 (quoted by Williams).

In this case it is difficult to imagine any other outcome than rupture, had pregnancy been allowed to continue, because of the predominance of fibrous over muscle tissue in the wall of the rudimentary horn. In reviewing the literature there are several cases reported of pregnancy going to term, but most cases ruptured early in pregnancy.

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Eden, T. W.: *Midwifery in the Home*, Brit. M. J. 1: 399, 1933.

There has been a gradual change in the relationships between general practitioner and midwife, and there will probably be a further change. New opportunities are consequently arising for the physician. Although a considerable amount of practice is being taken out of the physician's hands, he is becoming a consultant to the midwife.

It is estimated that midwives attend from 60 to 70 per cent of all the births in England with the proportion increasing each year. Since the physician acts in the rôle of consultant, more frequently his general obstetrical efficiency must increase correspondingly. In comparing mortality statistics, it is found that the English mortality rate between 1926 and 1931 was 4.26 per 1,000 births, while the maternal death rate of the midwives of the Queen's Institute of District Nursing during the same period was 0.42 per 1,000 births, with a total of 385,000 cases during this period. A physician was called in 26 per cent of these 385,000 cases. These cases were all delivered in the homes of the patients.

FRED L. ADAIR AND L. E. ARNOLD.

## DEATH FROM DELAYED CHLOROFORM POISONING\*

PAUL F. OLSON, M.D., AND DONALD C. BEAVER, M.D., ROCHESTER, MINN.

*(From the Department of Surgery, the Mayo Foundation, and Section on Pathologic Anatomy, the Mayo Clinic)*

IT HAS been known for many years that delayed toxic reactions sometimes follow anesthesia by chloroform. In 1905, Bevan and Favill reviewed the subject thoroughly, clearly set forth the nature of the changes produced by this reaction, and settled for all time the controversy concerning the ability of chloroform to excite lesions. Fatty changes, central necrosis, and even acute yellow atrophy of the liver were described as the principal lesions induced by this delayed toxicity. These facts have been confirmed repeatedly by experimental,<sup>1</sup> as well as by clinical observations, so that little can be added to the fundamental data contained in the many articles which have appeared. However, in the case which we report there are unusual features: the drug was taken by mouth with suicidal intent, renal function was severely impaired; extensive necrosis of the liver was present, and the chemical constituents of the blood were altered. These combine to make the case worth recording.

### REPORT OF CASE

A woman, aged forty-two years, ingested 3 ounces (90 c.c.) of chloroform with suicidal intent. Three hours later her family physician was called. He promptly aspirated her stomach, but nothing was obtained. The patient was under deep anesthesia for twelve hours as the result of the chloroform, and was in a drowsy state for another twelve hours. Twenty-four hours after taking the drug, she apparently had recovered completely. She was up and about and had resumed her normal activities. Her subsequent mental variations are a little difficult to evaluate, as the history obtained from the family suggests that the patient was the victim of manic depressive psychosis. The third day she was restless; the fourth day she became drowsy, and her skin took on an icteric tinge. She was admitted to the Mayo Clinic approximately four days after taking the chloroform. At this time she was irrational, with alternating periods of restlessness, and short periods of absolute quiet. She was moderately jaundiced. There were a few râles in the lungs but other physical abnormalities were not noted. The temperature was normal and the blood pressure was 94 systolic, and 64 diastolic. Urinalysis disclosed a moderate amount of albumin, a moderate number of pus cells, a trace of acetone, and a faint trace of bile. Examination of the urine for tyrosine was negative. The erythrocytes and the concentration of hemoglobin were within normal limits, but the leucocytes were increased to 23,300 in each cubic millimeter of blood. The value for sugar was 93 mg. (normal 90 to 120), and for urea, 156 mg. (normal 18 to 30), each per

\*Submitted for publication, November 23, 1933.

100 c.c. of whole blood; the carbon dioxide combining power of the plasma was 28 volumes per cent (normal 55 to 65), and the value for bilirubin was 10 mg. (normal 2) in each 100 c.c. of serum.

During the forty-eight hours that the patient lived after admission, she received 4 liters of 10 per cent solution of glucose intravenously, and voided less than 100 c.c. of urine. She was catheterized to make certain that the condition was that of anuria and not of retention.

Twenty-four hours after admission the value for urea had risen to 186 mg. in each 100 c.c. of whole blood and the value for bilirubin to 11 mg. in each 100 c.c. of serum. Apparently as the result of intravenous administration of solution of glucose, the carbon dioxide combining power of the plasma improved, and became 37 volumes per cent. Additional laboratory data were as follows: inorganic sulphates 44 mg. (normal 2 to 5) in each 100 c.c. of serum, uric acid 11.1 mg. (normal 2 to 4) in each 100 c.c. of whole blood, cholesterol 38 mg. (normal 165 to 190) in each 100 c.c. of plasma, and cholesterol esters 10 mg. (normal 110 to 135) in each 100 c.c. of plasma.

At necropsy, the lungs revealed extensive edema with confluent portions of consolidation typical of bronchopneumonia. The heart and pericardium were normal. The entire gastrointestinal tract, including the esophagus, appeared normal, except

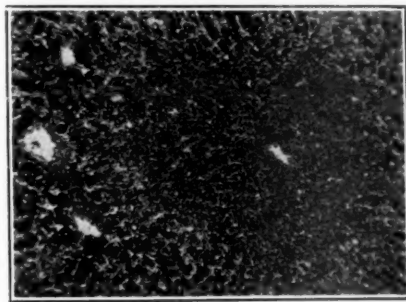


Fig. 1.—Central necrosis of the liver (hematoxylin and eosin).

the first portion of the duodenum, in which there were small, superficial areas of ulceration. The liver weighed 1,430 gm. The surface was smooth, mottled light red and yellow, and its consistence was moderately decreased. On sectioned surface lobular markings were obscure. There were multiple, dull yellow zones, the size of a pinpoint, throughout the liver, apparently zones of necrosis within hepatic lobules. The kidneys weighed, together, 309 gm. The cortices were somewhat swollen and cloudy, and parenchymal markings were obscure. Other organs were essentially normal. The brain was not examined.

Microscopically, sections of the liver disclosed severe central necrosis, uniformly present throughout all portions (Fig. 1). In the zones of necrosis the outlines of hepatic cords and cells were partially preserved. The cells were small. The cytoplasm was intensely acidophilic and granular, and was interspersed with multiple fine droplets which were revealed as lipoids by scharlach R stain. Nuclei were rarely present in the cells, although an occasional pyknotic or karyorrhetic nucleus was identifiable. In the peripheral third of the lobule the cells were less severely injured. The change to this peripheral third was abrupt. Here the cells were irregularly swollen. The cytoplasm was faintly stained with eosin, slightly granular, and vacuolated. Nuclei were essentially normal. The vacuoles of these cells were also demonstrated as lipoids by scharlach R stain. Sinusoids were irregularly congested. The reticulo-endothelium and bile ducts appeared normal. Polymorpho-

nuclear leucocytes and lymphocytes were observed in collections which were especially prominent in the periphery of the necrotic zone and in the periportal connective tissue. Occasionally more extensive changes were present, especially in subcapsular lobules, in which there was complete necrosis of all hepatic cells, with clearing of the necrotic detritus, leaving dismantled reticulo-endothelium, sinusoids, and bile ducts to mark the position of a former hepatic unit.

In sections of the kidneys the convoluted tubules revealed severe, apparently selective, retrogressive changes. The tubular cells were swollen, the cytoplasm was intensely acidophilic and granular, with here and there hydropic degeneration. In addition, scharrlach R stains disclosed small fat droplets in the basal portions of the cells. Nuclei of some of these cells revealed pyknosis or karyorrhexis. Granular and hyaline casts were fairly abundant in convoluted and collecting tubules, with also collections of erythrocytes sometimes present in similar positions. Glomeruli appeared normal; the capillary loops frequently were engorged with erythrocytes.

The microscopic preparations of the lungs disclosed intense capillary congestion, edema, hemorrhage, and patches of bronchopneumonia. Preparations of the duodenal ulcers disclosed them to be acute, focal zones of necrosis which involved the mucous membrane and the submucosa, with mild polymorphonuclear cellular reaction at the base.

#### COMMENT

The hepatic changes were sufficient to bear the designation of acute atrophy. The parenchymal injury of the kidneys was no doubt sufficient to explain the almost total cessation of urinary function, with elevated values for blood urea, uric acid, and inorganic sulphates; otherwise the altered physiology of these organs is difficult to account for, because glomerular injury, if present at all, was too mild to be disclosed by microscopic study. The elevation of serum bilirubin with a direct van den Bergh reaction was in conformity with the clinical and anatomic evidence of hepatic injury. Reduction of cholesterol and cholesterol esters in the blood also may be explained on this basis, since in severe hepatic injury from other causes there is often diminution of these substances in the circulating blood.

The evidence indicts chloroform only circumstantially as the cause of the lesions of the kidneys, for the reason that similar renal changes are associated with jaundice when due to other causes. However, in favor of chloroform rather than jaundice as the cause, is the observation that both jaundice and anuria appeared in this case at approximately the same time. There is a certain amount of experimental, as well as clinical evidence, which indicates that chloroform may induce lesions in the kidneys, as well as in the liver. In this regard may be cited the observations of Bevan and Favill, Offergeld, Stander and Anderson.

The studies of the blood in this case are in agreement with those reported by Stander, who reported "an increasing nitrogen retention, low chloride concentration, marked uric acid increase, decreased alkali reserve to a level of true acidosis, a high concentration of amino acids and a sugar level at or slightly below normal."

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## FATAL ECLAMPSIA AT THE FIFTH MONTH WITH COMPLETE AUTOPSY\*

ROLAND D. PORTER, M.D., JENKINTOWN, PA.

IN 1928 Fueth reported a case of eclampsia during the fourth month of pregnancy and collected 56 cases, only 31 of which were at all complete. There were 11 deaths with autopsies, some of which presented a picture of acute nephritis. Shearer also feels that many of the cases early in pregnancy are nephritic and not eclamptic.

It is the purpose of this report to present a case of eclampsia occurring during the fifth lunar month of pregnancy, a case which ended fatally, and at autopsy exhibited many interesting pathologic changes supporting much of the etiologic work in regard to the cause of eclampsia.

M. W., aged forty-three, white, married, was admitted to Abington Memorial Hospital Jan. 14, 1933, at 2 P.M., and died Jan. 15, 1933, at 10 A.M.

Patient had last period in late July and since has not been well. She has complained of headache intermittently all during the summer months and has been under care of her family physician. These headaches have become more severe during the last week, and there has appeared some edema of the lower extremities. During the last twenty-four hours before admission she has not been without headache. Lately her urinary output has been low.

As a child, she had measles, chickenpox, and mild scarlet fever; at thirteen an attack of acute rheumatic fever lasting about four months, during the greater part of which many of her joints were badly swollen, and she had high fever. Had several attacks of biliousness, when she became sallow but never had any decided jaundice. Menstruation normal.

General physical examination negative. Blood pressure 192/100. No radical sclerosis. Uterus enlarged to two-thirds the distance from symphysis to umbilicus. Very slight edema of the ankles present. Vaginal examination showed uterus enlarged to size of five and one-half months' pregnancy. Cervix closed.

*Urine*.—Acid, 1033; sugar, negative; heavy cloud of albumin; sediment on centrifuging showed fine and coarse granular casts, epithelium and white and red blood cells. *Blood Chemistry*.—Chlorides, 480; sugar, 89; blood urea nitrogen, 15; CO<sub>2</sub>, 48; cholesterol, 265; Wassermann and Kahn tests, negative.

Immediately upon admission the patient was purged, given sedatives; intake of fluids limited, and intravenous glucose administered in concentrated solution. Her blood pressure constantly rose, however, until she went to sleep near midnight. Following a vomiting spell early in the morning, she sank into a stupor from which she did not emerge until death occurred at 10:20 A.M.

\*Read at meeting of the Obstetrical Society of Philadelphia, December 7, 1933.



*Autopsy Findings.*—Heart: Simple varicose mitral valvulitis; petechial hemorrhages; early coronary sclerosis; slight myosclerosis (probably inflammatory in origin); cloudy swelling; right-sided dilatation. Aorta: Moderate degree of arteriosclerosis. Lungs: Passive congestion and edema.

Spleen: Weighed 260 gm. (moderate enlargement). Diffuse, soft, fibrous adhesions; follicular hyperplasia; low grade chronic interstitial splenitis. Pancreas: Low grade interstitial pancreatitis. Duodenum: Submucous pinpoint hemorrhages. Upper ileum: Few small subserous hemorrhagic areas.

Uterus: The size of five and one-half months' pregnancy. No noteworthy lesions. Placenta: Moderate thickening of villi due to proliferation of young connective tissue. Areas of necrosis. Ovaries: Fibrosis and small simple cysts. Kidneys: Moderate degree of sclerosis of the renal arteries, passive congestion, areas of chronic glomerulonephritis, simple nephrosis. Urinary Bladder: Showed hemorrhagic areas of the mucosa. Liver: Weighed 1,920 gm. and was firm in consistency. The edges were sharp. The capsule was smooth and not thickened. The color was mottled grayish to purplish brown with irregular blotches of purplish red. These blotches varied in size from pinhead to 3 cm. and to 5 cm. in diameter. They were most numerous over the right half of the right lobe and resembled in appearance the hemorrhagic stages of acute yellow atrophy. The capsule was covered with soft, veillike, fibrous adhesions. On section the surface was nutmeg in appearance, and the amounts of blood were diminished. Section surface was studded with irregular confluent blotches shading from reddish to purplish red. The reddish areas were fairly evenly distributed over the section surface. Microscopically there were seen irregularly distributed areas of necrosis of liver cells. The protoplasm of these cells seemed to fade away leaving a network of the outlines of the cells. The hemorrhages occurred in the areas of liver cell necrosis. There was round cell infiltration around the bile ducts and the blood vessels at the periphery of the lobules. There were many small areas which contain dense, irregular, hyaline, eosin staining masses (not amyloid), probably condensed fibrin replacing liver cells destroyed at an earlier date. Liver cells in the nonnecrotic areas were somewhat cloudy in appearance. Diagnosis: Acute necrosis of the liver cells with extensive hemorrhages (hemorrhagic stage of acute yellow atrophy), chronic hepatitis, cloudy swelling, chronic perihepatitis.

Brain: Shows slight edema and engorgement of the veins. The interior surface of the cerebellum shows hemorrhagic areas. Pituitary: Shows a small cyst situated in the posterior portion of the anterior part and in the pars intermedia. Otherwise there are no lesions.

*Postmortem Bacteriologic Studies.*—Culture from the liver. Hormone broth showed staphylococcus-like organisms. Brain broth remained sterile. Culture of bile remained sterile. Culture of the spleen: Brain broth showed nonhemolytic streptococci. Hormone broth culture showed hemophilic, hemolytic, pleomorphic gram-negative bacilli in the threads.

Postmortem blood urea nitrogen, 25 mg. per 100 c.c.

Five cubic centimeters of twenty-four-hour culture of streptococcus from the spleen were injected in two rabbits intravenously. The rabbits did not show any rise in temperature and remained at all appearances in healthy condition. When the rabbits were killed on the fourth day, their livers revealed microscopically changes similar to those observed in the patient.

#### DISCUSSION

The liver changes in this case are those which are held by Dieckman, Williams, and others to be those characteristic of eclampsia.

Numerous writers among whom are DeLee, Talbot, Ivens, Johnston and Johnson and Nickolas, Albert, and Carey subscribe to the idea that bacterial infection plays a

rôle in the etiology of eclampsia. It seems that the detoxifying powers of the liver in this case were so exhausted by the continual infection from the spleen that its margin of safety has been broken earlier than is common. Modern methods of artificial growth of bacteria may show an increasing number of cases which are harboring virulent organisms in such a situation that they can readily play an important rôle in these cases.

Several investigators, among whom are Lawrence, Corwin, and Herrick, have felt that there is a relation of eclampsia to cardiovascular failure and that cardiac defects and anemia make a woman especially susceptible to this disease. The cardiovascular changes in this case with incompetent valves, chronic myocardial changes, and arteriosclerosis were very likely to have added to the susceptibility to eclampsia.

That those individuals who suffer from kidney disease are more susceptible than the normal to eclampsia has long been known. The arteriolar nephrosclerosis of this case places it in this unfortunate group.

#### SUMMARY

The autopsy findings in this case of eclampsia in the fifth month of pregnancy suggest that an individual who has chronic cardiovascular changes, chronic renal changes, and whose liver detoxifying powers are already under considerable load, will be particularly susceptible to eclampsia.

305 MEDICAL ARTS BUILDING

### PRENATAL PREVENTION OF POTENTIAL HEMORRHAGIC DISEASE OF THE NEWBORN, SUPPLEMENTARY REPORT

I. N. KUGELMASS, M.D., AND JOHN E. TRITSCH, M.D., NEW YORK, N. Y.

(From the Department of Pediatrics, The Fifth Avenue Hospital)

THE tendency of certain mothers to give birth to babies with hemorrhagic disease is not uncommon. It may become manifest with the first born or appear suddenly in subsequent children. The occurrence of true hemorrhagic disease of the newborn seems much less prevalent in the last few years. The recognition and treatment of the condition are so simple that there is no great concern in prognosis. But those newborns with hemorrhagic disease from mothers who have transmitted the condition periodically, are least responsive to postnatal therapy. Diagnostic and therapeutic approaches can now be made through prenatal study.

Examination of the mother's blood during pregnancy reveals a characteristic blood picture. We have been able to make such a correlation by determining the blood content in the essential clotting constituents. We have observed in newborns with true melena that the dominant deficiency in the blood is a diminution in the prothrombin content. Occasionally the fibrinogen content may be diminished or the antithrombin slightly increased. This is apparently the reflection of the maternal blood with which it is always in equilibrium. This type of congenital predisposition to a hemorrhagic tendency may thus be predicted by examination of the maternal blood whenever there has been previous evidence of hemorrhagic disease in the newborn.

Proof of the prenatal prevention of hemorrhagic disease in the making is afforded by a carefully controlled human experiment. A mother had given birth to four successive newborns with severe hemorrhagic disease. She was observed by



the same obstetrician in the same hospital and postmortem examinations of the newborns were made by the same pathologist. We previously reported<sup>1</sup> the recognition of potential hemorrhagic disease during her fifth pregnancy and were able to prevent the development of hemorrhagic disease by a high protein diet during the prenatal period. The fifth newborn was normal and is now about six years of age without ever having manifested the slightest hemorrhagic symptomatology. The sixth pregnancy was characterized by a similar hemorrhagic tendency as revealed by biochemical study of the maternal blood. But the mother refused nutritional therapy, and we did not coerce her in order to obtain a control newborn without prenatal supervision. This sixth newborn showed severe hemorrhagic disease and died of uncontrollable hemorrhage. During her seventh pregnancy we proceeded with nutritional therapy exactly as during her fifth pregnancy, her blood having shown similar hemorrhagic tendency. The seventh newborn was perfectly normal and free from any semblance of hemorrhagic symptomatology.

The relation of nutrition and hemorrhagic disease to the newborn has been envisaged from the following considerations. On studying the blood of patients routinely for the content of clotting substances, we devised simple methods<sup>2</sup> for their determination as well as an index of blood clotting function for characterizing the tendency of a patient to bleed or to thrombose. We applied this procedure<sup>3</sup> and observed that the prothrombin and fibrinogen constituents would increase following the administration of very high protein diets, particularly viscera and gelatin. Such a relationship is explicable on the basis of the protein nature of these two clotting substances, both synthesized in the liver. The recurrence of variant hemorrhagic symptoms in older children has likewise been correlated with a diminution of these clotting constituents and been cleared by the administration of a high protein diet. Russel Haden<sup>4</sup> and George Minot<sup>5</sup> report similar hemorrhagic symptoms in adults cleared by the same procedure. The clinical manifestations in women with a hemorrhagic tendency include recurrent nosebleeds and easy bruising. Although these symptoms are too frequently neglected they have been cleared by the administration of a high protein dietary and an examination of their blood has previously shown a low prothrombin content.

We present this ten-year study of a striking human problem demonstrating the predictability of hemorrhagic disease in the newborn from a study of the maternal blood. We have thus been able to detect early in pregnancy a hemorrhagic tendency which becomes manifest in the newborn. A study of the maternal clotting constituents of the blood has given us an insight into the mechanism of development of hemorrhagic disease in the newborn. We have further been able to prevent this disease by prenatal treatment through the dietary. This procedure represents a new approach in the perfection of the newborn through specific treatment in utero.

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1060 PARK AVENUE

## TREATMENT OF FUNCTIONAL UTERINE BLEEDING WITH EXTRACT OF PLACENTA\*

ALEXANDER GABRIELIANZ, M.D., CHICAGO, ILL.

(From the Department of Obstetrics and Gynecology, Rush Medical College of the University of Chicago)

IN THE endocrine treatment of functional bleeding, I have used the water-soluble extract of placenta prepared by Dr. Mark T. Goldstine, which is a preparation similar to the placental hormone of Collip.

The treatment consisted of subcutaneous injections of 2 c.c. of placental extract, 100 rat units each, on alternate days, until the bleeding stops. The quicker the response, the shorter the time of treatment. If the intervals of bleeding are short, we start the injections immediately after the bleeding begins, otherwise we give the injections on the fourteenth day after the first day of the last menstruation.

We have treated 24 patients, the youngest eighteen years old, the oldest, forty-eight. The greatest frequency was between the ages of twenty-two and thirty. There were 10 unmarried patients, 4 having intact hymens. There were 14 married, 3 of whom were sterile; 11 had had from one to four children each, the predominant number being two or three. The duration of the hemorrhage varied from one or two months to two or four years with intervals. During treatment not a single patient became pregnant. In 3 patients bleeding began after childbirth.

No characteristic constitutional features were found.

The complaints of the patients were mostly general weakness, irritability, loss of strength, vertigo, often palpitation of the heart, and tremor of the hands. Bimanual examination showed the uterus in virgins and nulliparas to be small; both ovaries, when they were easily palpable, were often enlarged, due probably to persistent nonrupturing follicles, and nodular.

The types of bleeding observed were menorrhagia, metrorrhagia, and polymenorrhea. The quickest result was obtained in four cases of polymenorrhea, each of whom responded by menstruating at longer intervals after several injections of placental extract. The most difficult cases were those with metrorrhagias of long duration. In one case of metrorrhagia of two years' duration in a woman, aged thirty-one years, ten years married and sterile, it required five months of treatment before menstruation was brought to normalcy.

In one case, a twenty-seven-year-old unmarried woman, whose first menstruation occurred at twelve, there was severe menorrhagia of three months' duration. Twenty-eight injections of placental extract, 2 c.c. each time, were used during four months of treatment. As a result of over-luteinization, the patient developed amenorrhea for two months.

In our series of 24 patients, one did not respond to treatment at all. She was curetted, but the endometrium did not reveal any characteristic changes. This patient stopped bleeding after curettage and has had two regular menstruations since. At present we still have 5 patients under observation and one under treatment. This patient, twenty-eight years old, had her first menstruation

\*Read before the Chicago Gynecological Society, November 17, 1933.



at the age of twelve years, at which time she was tall, large, and weighed 160 pounds. At the age of seventeen she started to menstruate irregularly. This condition has become aggravated during the last four years; menstruation lasts from nine to sixteen days, and at times she has flowed the entire month.

We have not seen any ill effect except in one case. After the first injection the patient became suddenly pale and had palpitation of the heart and tremors of the hands. This lasted about ten minutes. The reaction was very similar to the Goetsch test and was probably due to stimulation of the suprarenal gland.

In using placental extract in 93 cases, Goldstine reports 78 successfully treated. Some failures occurred due to errors in diagnosing a small submucous fibroid and in some, to unknown causes. Five patients who failed to respond were operated upon, and from these patients seven ovaries were removed, which histologically showed a marked tendency to the formation of corpus albicans and excessive follicle formation tending to luteinize without rupture. Goldstine states that in his cases he found no cause for bleeding in the endometrial picture. The women who bled had a different type of endometrium. He found that polypoid degeneration of the endometrium is associated with polypoid degeneration of the ovary.

The main factor in checking uterine bleeding is the formation of corpus luteum. In regard to the action of the placental extract, it seems to be purely a luteinizing hormone. Smith and Engle recently injected adult monkeys with ten to fourteen injections of follicle-stimulating sheep pituitaries. Simultaneously, with the last four of these injections, theelin, 100 rat units, was given daily. Following the injections the uterus became large. Bilateral ovariectomy was performed and, contrary to the usual occurrence following such an operation, bleeding did not occur because the animals had been treated with progestin (made from corpus luteum). By using progestin, bleeding has been prevented in various animals for from ten to twenty-eight days after the double stimulus to bleeding afforded by bilateral ovariectomy and cessation of estrin treatment.

In conclusion I believe that the placental extract is the strongest known luteinizing hormone.

The use of the placental extract in the cases of functional bleeding in young or in sterile women must be limited.

25 EAST WASHINGTON STREET

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**Quadras-Bordes: Metrorrhagias of Ovarian Origin Treated With Insulin, Med. Ibera 1: 775, 1933.**

Four cases of metrorrhagia are reported, which had been treated with ovarian and thyroid extracts, ergot, calcium chloride, etc. When they did not respond, insulin was given with excellent results. It was found that if insulin was given daily throughout the whole menstrual period in two doses of 20 and 15 units or 20 and 20 units, the hemorrhage ceased and after such treatment for several months insulin could be discontinued. Thirty-five units of insulin in two doses of 20 and 15 units seemed to produce the best results.

JAMES M. PIERCE.

## CONGENITAL RHABDOMYOMA OF THE HEART

CARL H. ILL, M.D., AND JOHN W. GRAY, M.D., NEWARK, N. J.

(From the Department of Obstetrics and Pathology, Hospital of St. Barnabas)

**C**ONGENITAL rhabdomyoma of the heart is an exceedingly rare tumor. This case is being reported, therefore, for this reason and because, clinically, the baby presented the signs of a cranial hemorrhage.

Mrs. F., aged twenty-four years, Jewish, first consulted me Jan. 12, 1934, being pregnant the second time. Her past history was essentially negative.

Her first pregnancy two years before was normal and she had a spontaneous delivery after being in labor twelve hours. The baby did well for two days, when it suddenly showed signs of cranial hemorrhage, and in spite of lumbar puncture, numerous infusions and transfusions, it died on the tenth day. There was no autopsy; clinical diagnosis was cranial hemorrhage according to the doctor who took care of her.

At the time of the first visit, her general physical condition was entirely normal; weight 134 pounds, blood pressure 120, urine negative. Her pelvis was of the normal female type. She had spent a great deal of time in the sun; back, arms, and legs being very tanned. Position of the child was L.O.A., head in midpelvis, cervix dilated 2 cm. two weeks before delivery. She delivered on July 27, spontaneously, of a male child, weighing 7½ pounds. Pains never were hard and she was in labor only five hours. The baby cried immediately after being born, heart rate being 130 and rhythm normal. The baby did very well for forty-eight hours; color was good; the only abnormal feature being that he would not nurse well. Suddenly, just forty-eight hours after birth, the baby was cyanotic, limp, and flaccid, gasping for breath, and had a small stridulous cry. On examination lungs were clear, heart sounds were quite distant, and he had a peculiar gallop rhythm. In the belief that this was a cranial hemorrhage, lumbar puncture was done, fluid under no pressure and clear. The child was given oxygen and 5 per cent carbon dioxide, lived an hour and suddenly died.

*Autopsy.*—The general appearance was that of a well-developed infant two days of age, somewhat cyanotic. The external examination revealed no skin lesions, evidence of traumatism or enlargement of the superficial lymph nodes.

The surface vessels of the brain were congested but no external or internal hemorrhages or sclerosis were observed.

There was no fluid in the pleural cavities. The bases of the lungs were congested and the upper lobes were spotted with red semisolid areas. The thymus was normal in size and consistency. There was no enlargement of the mediastinal lymph nodes. The abdomen contained an excess of straw colored fluid. The stomach and intestines appeared normal. The liver and spleen were enlarged apparently from congestion. The suprarenals and kidneys showed no pathology.

There was no excess of fluid in the pericardial sac. The heart presented a peculiar, enlarged, deformed appearance. Bulging from the anterior surface, particularly from the left ventricular wall and intimately associated with it, there was a large yellowish tumorlike mass. Beneath the pericardium small yellow colored nodules were seen. The heart weighed 45 grams.

On opening the heart, the right auricle and ventricle were distended with clotted blood. The large bulging, irregular, oval mass in the left ventricle and anterior portions of the interventricular septum measured 4.5 by 3.5 cm. The tumor was encapsulated and the cut surface was grayish yellow in color and its consistency

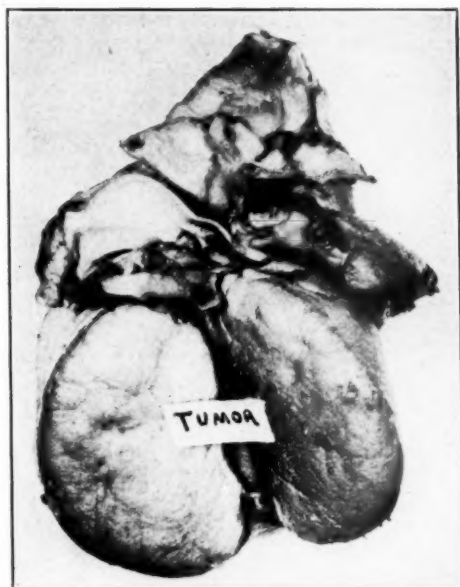


Fig. 1.—Heart with the large encapsulated tumor of ventricular wall incised and laid open.

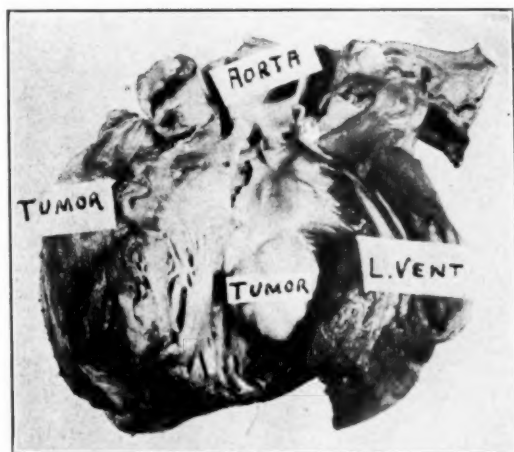


Fig. 2.—Heart with left ventricle exposed showing a small part of the large tumor to the left, smaller tumor partially occluding the atrophic ventricle and the narrowed aortic orifice.

spongy. The left ventricular cavity was almost completely filled by another globular tumor about 1.5 cm. in diameter. A very small growth 0.5 cm. in diameter was present in the interventricular septum and a few tiny yellow nodules were found beneath the endocardium. The musculature of the left ventricle was only 3 mm. in

thickness. The mitral valves were poorly developed, the left auricle was extremely small, and the aortic valve was narrowed (12 mm. in diameter).

The wall of the right ventricle measured 5 mm. in thickness, the pulmonary valve 2 cm. in diameter. The columnae carinae of the ventricle and the papillary muscles

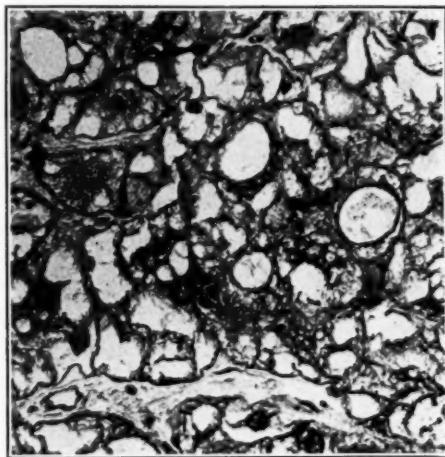


Fig. 3.—Photomicrograph of tumor showing numerous vacuoles and typical cells.  $\times 250$ .

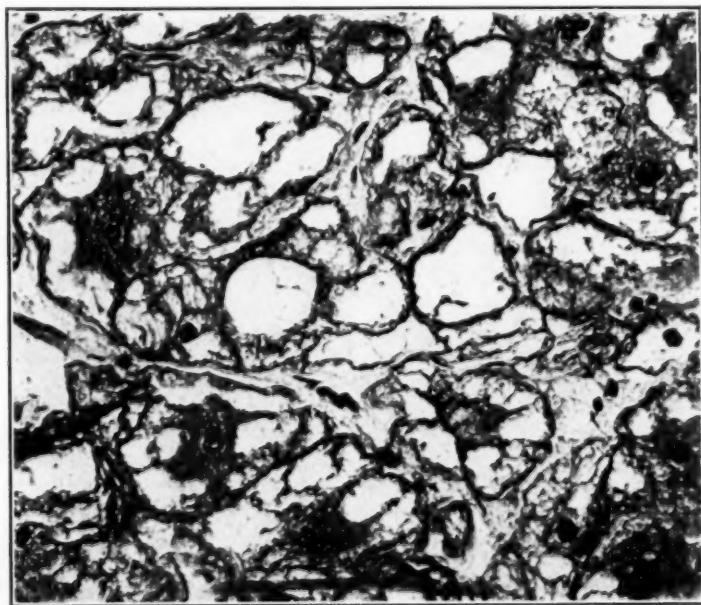


Fig. 4.—Photomicrograph of tumor. Note "spider cells" with thick protoplasmic walls and vacuoles lying between cell processes.  $\times 450$ .

were markedly hypertrophied. The bicuspid valve was dilated and measured 4 cm. in diameter. The right auricle showed a marked hypertrophy of the musculature and dilatation of the cavity.

The alveoli of the lungs contained an exudate which was largely composed of blood and some of the bronchioles contained blood. The liver was congested. The sinusoids

of the spleen were congested with blood. The thymus and suprarenal were normal. Kidney tubules moderately swollen and congested. Unfortunately the brain was not preserved for microscopic examination.

Heart examination: Sections from the large tumor showed it to be surrounded by a dense fibrous capsule. The capsule was surrounded by essentially normal myocardium. The spongy tumor presented numerous large vacuolated spaces irregular in size. Some of the spaces were empty while others contained large centrally placed cells with numerous processes extending outward in the spaces or to the thick protoplasmic walls of the spaces (Seiffert likened the cells to spiders in their webs and the characteristic cell of this tumor has since been called the "spider cell"). The processes were striated. The cells contained one, and sometimes two nuclei. Connective tissue trabeculas surrounded the spaces.

The histologic structure of this tumor was characteristic of congenital rhabdomyoma of the heart.

This case is the fourth reported in American literature and the forty-fourth on record. An excellent critical review of the subject was made by Farber<sup>2</sup> in 1931 in connection with his case report. Although the tumor is observed most frequently in infants a few days or a few months of age, 17 of the 44 cases were one to fourteen years of age and 6 occurred in adults. Tuberous sclerosis was present in 25 out of 33 cases where the head was mentioned. To a lesser degree there have been reported kidney tumors of various types, adenoma of the skin and certain other developmental anomalies.

The true nature of the tumor as the beginning of muscle fibril formation was established by Wolbach.<sup>3, 4</sup> He showed that the vacuoles were intracellular, that the cross striations were formed of fuchsinophil granules grouped in the sarcous elements, and that longitudinal striations were made up of alternating sarcous elements and basophilic fibrillary material. He also showed that similar cells may be found in the fetal myocardium. The resemblance of the cells to Purkinje's cells and those of the conducting bundles of the heart was mentioned by Knox and Schorer.<sup>5</sup> Ponfick<sup>6</sup> called attention to the association of rhabdomyoma of the heart and tuberous sclerosis and described a diffuse fibrillary gliosis limited to the gray matter. Bonome<sup>7</sup> traced the pathogenesis to fetal malnutrition resulting in fibrous overgrowth of the heart and separation of embryonal cell nests.

While the interest of these rare conditions lies partly in their clinical significance, their chief interest to the pathologist lies in the realm of pathogenesis. We now know the nature of congenital rhabdomyoma of the heart but until the deviations from the normal in fetal growth can be explained, the etiology and pathogenesis remain obscure.

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## OVARIAN PREGNANCY\*

SAMUEL M. DODEK, M.D., M.A., WASHINGTON, D.C.

(From the Department of Obstetrics and Gynecology, School of Medicine,  
George Washington University)

OF THE many cases referred to as ovarian pregnancies and reported in the literature, only 52 seem to have rigidly fulfilled the criteria laid down by Speigelberg in 1878, to establish definite diagnosis. Eighty-seven cases reviewed by Wollner in 1932 revealed not over 48 definite ovarian gestations. The case which I am about to report, presents sufficient microscopic and macroscopic evidence of a primary type of extrauterine pregnancy in the ovary.

Mrs. E. C., white, aged nineteen years, was admitted at 6 A.M. on Nov. 1, 1932. She complained of pain in the hypogastrium, accompanied by a slight yellow vaginal discharge. She said the pains began early in the morning of the day of admission and were of a cramplike nature, the discharge coming on with the onset of pain. She gave no history of ever having had a similar attack, and there had never before been a noticeable vaginal discharge. She had had no chills, no nausea or vomiting and no fever. Her family history was irrelevant. Her past medical history was essentially negative except for diphtheria at the age of seven.

Her menses, of the twenty-eight- to thirty-day type and lasting seven days, began at the age of eleven, and were painless. She had been pregnant once, delivering a full-term living child about two years before. There had been no miscarriages. Her last menstrual period, occurring thirteen days before admission, lasted seven days and was normal in every respect.

The patient desired to go home on the day of admission because the pain had suddenly disappeared very shortly after she was admitted, and because of the absence of any other symptoms and a general feeling of well-being. However, I observed that the patient's color was exceptionally pallid. Questioning revealed that she herself noticed that with the onset of pain she became suddenly pale, but that the pallor was not progressive. In view of this the patient was urged to stay for observation and study, since a differential diagnosis, seriously considering an atypical ruptured ectopic pregnancy with controlled hemorrhage, had to be made.

General physical examination showed that the patient was well nourished and developed, and was slightly obese. Abdominal examination revealed no tenderness or rigidity, or shifting dullness. The uterus was barely palpable just above the margin of the symphysis. Speculum examination revealed a bilaterally lacerated and eroded cervix which was not discolored. The mucous membrane of the vagina seemed normal. The right tube was palpable but not tender, but there was a slightly tender mass in the left vaginal fornix. There was no bleeding and the discharge was very slight.

The blood pressure on admission was 130/60, pulse 96, and respiration 20. The blood count was 2,490,000 red blood cells and 12,000 white blood cells, small lymphocytes 10 per cent, large mononuclears 3 per cent, polymorphonuclears 87 per cent. The urinalysis was normal. The patient remained at rest in bed under observation for ten days, during which time her temperature varied but 0.8° from normal on the sixth day, remaining normal thereafter. The pulse rate averaged 80. I per-

\*Presented at a meeting of the Washington Gynecological Society, January 27, 1934.

formed a laparotomy on the eleventh day after admission under general anesthesia, through a midline incision. A bluish discoloration of the peritoneum suggesting the presence of blood within was noted. Exploration of the abdominal cavity revealed a blood clot in the culdesac and a rent on the posterior surface on the left ovary about 1 cm. long (Fig. 1), the edges of the wound being everted as having given way to an explosive force. The infundibulopelvic ligament on the left side supported the ovary and was attached to it. The left tube and the right tube and ovary appeared normal.

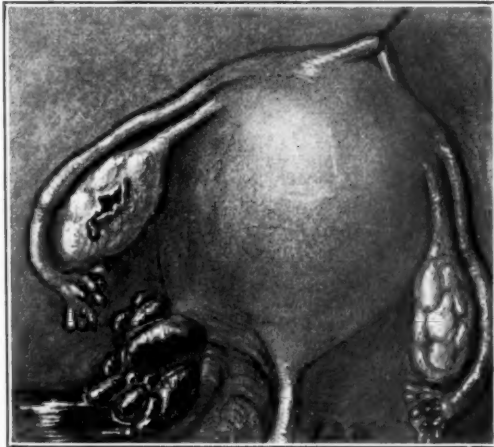


Fig. 1.—A diagrammatic sketch of the ruptured left ovary in situ with blood clots as seen at the time of operation.



Fig. 2.—Cross-section of removed ovary, showing the large corpus luteum of pregnancy, and a portion of the attached blood clot at the right.

The blood clot was removed. The ovary was excised and the raw edges of the base were buried between the leaves of the broad ligament. The left tube was not disturbed. The abdomen was closed without drainage.

For nine days the patient's postoperative temperature ranged from 100° to 102.5° F. without any marked elevation of the pulse. On the seventeenth day the patient was discharged well, the wound completely united.

A follow-up pelvic examination made ten months postoperatively, revealed the left side to be free of pain or any palpable adhesions; the right ovary had become

somewhat cystic. The abdominal scar was well healed and the menstrual periods had been normal.

The removed ovary measured 3 cm. by 8 mm. and on its posterior surface there was a rent about 1 cm. long. The blood clot which was removed from the peritoneal cavity measured 6 cm. by 10 mm. Microscopic examination showed a large corpus luteum of pregnancy (Fig. 2). Section through the blood clot showed a considerable amount of blood in which were scattered chorionic villi. No attachment of placental tissue to the ovary was found. The pathologic examination was made by Doctor H. H. Leffler.

#### SUMMARY

A case of an early ectopic pregnancy presenting atypical symptoms, which was primary in the left ovary, is reported. Rupture due to growth caused its expulsion into the abdominal cavity.

The presence in an otherwise normal pelvis of a ruptured ovary from which had been expelled a blood clot, the former revealing a large corpus luteum of pregnancy and the latter chorionic villi, seems to be indisputable evidence of a primary ovarian pregnancy.

1835 EYE STREET, N. W.

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### PLACENTA PREVIA COMPLICATING TWIN PREGNANCY

JOSEPH F. GALLAGHER, M.D., C.M., F.A.C.S., AND LEONARD D.  
HEATON, M.D., FORT SAM HOUSTON, TEXAS

(From the Surgical Service, U. S. Army Station Hospital, Fort Sam Houston, Texas;  
Lieut. Col. Joseph Casper, B.S., M.D., F.A.C.S., Chief of Service.)

IT HAS been aptly stated that placenta previa in twin pregnancy endangers three lives. There is little precedent to follow in the treatment of this complication. We report a case of partial placenta previa complicating bi-oval twin pregnancy, at or near term, treated by version and slow extraction of first twin; version and extraction of second twin; followed by manual removal of second placenta, with recovery of all three patients. It is the first time we have encountered this condition and the various texts with which we are familiar make little or no mention of it.

#### REPORT OF CASE

A. E., wife of a soldier, aged forty, born in Mexico, a para viii, was admitted to hospital Sept. 3, 1933, complaining of slight, painless bleeding for one month. She had attended the prenatal clinic only twice, the last visit being July 17, 1933. Up to this time there had been no vomiting, edema, or bleeding, but she complained of occasional headache. Her weight was 134 pounds and her blood pressure was 110/70. The urine, Wassermann, and Kahn tests were negative. Her last period was on Dec. 17, 1932, quickening occurred in April, and the estimated date of confinement was Sept. 24, 1933.

The patient was married in 1916 and there was no history of severe illnesses or operations. Her menstruation began at the age of twelve and occurred regularly every twenty-eight days with no pain. She had had three abortions and seven full-term children: all single pregnancies. All deliveries were normal without complications or lacerations. The age of the oldest child was sixteen years and the

youngest seventeen months. One child died of pneumonia at seven months, the others were alive and well. The birth weights of the children varied from seven to eleven pounds.

Twins were diagnosed by abdominal palpation and the diagnosis confirmed by x-ray. The first twin occupied the left half of the uterus and was a vertex presentation with the occiput anterior and to the left. The second twin was on the right and also a vertex.

At the time of admission there was no bleeding and no contractions. Her blood pressure was 120/80, pulse 84, red blood cells numbered 3,900,000, hemoglobin 75 per cent. The head of the first twin was floating above brim, cervix soft and boggy, head could not be reached per rectum. At 8:15 P.M. on Sept. 4, 1933, she had a painless gush of blood estimated to be between 200 and 300 c.c.

Under combined nitrous oxide-oxygen-ether anesthesia, the diagnosis of placenta previa was confirmed with the whole hand in the vagina and two fingers inserted into the cervix. The edge of the placenta was felt coming from the patient's left and posteriorly, and extending more than halfway across the os. The extreme edge of the placenta was tough and fibrous and probably, before effacement and dilation, had been attached to opposite side of cervix. The head was ballotable and membranes were unruptured. The membranes were ruptured artificially as far away from the placental edge as possible and a No. 6 Voorhees' bag was inserted intraovularly and the head displaced upward. The cervix was effaced, very soft and dilated about 4 cm. When the bag was one-third full, the connection of the syringe for filling the bag became unserviceable and could not be used. Unfortunately, there was no additional connection ready sterilized at hand.

The manipulation and insertion of the bag had brought on moderate bleeding which could be controlled by digital pressure. The bag was withdrawn and the posterior leg brought down with complete control of bleeding. During the effort to reach a foot, the left hand prolapsed, but was ignored. The presence of the second twin interfered somewhat with the maneuver but by pushing up the head, which could be felt in its own sac, with the internal hand and pushing the first head upward and to the patient's left with the external hand, the version was completed. The anesthetic was continued and intermittent, firm traction was put upon the leg. The cervix proved to be dilatable, so a slow extraction was possible. When the breech was just about to make its way through the cervix, the cord was felt on the perineum of the baby. The baby's life was despaired of, as rapid delivery could not be done without danger to the integrity of the cervix. The cord was pulsating. It was loosened and gently and gradually pushed upward over the flexed thigh within the uterus and protected with the fingers from pressure. The breech finally eased through the cervix and the baby delivered to the umbilicus. The cord was disengaged and the anterior leg secured. The right or anterior arm, which was somewhat extended, was extracted first and then the posterior arm without change of position of the baby. The cord was still pulsating. The head was easily brought to the pelvic floor and delivered by Martin-Wiegand maneuver at 9:45 P.M. The heart was beating strongly but slowly, about 40 or 50 per minute. The face was suffused and cyanosed and the baby made no effort to breathe but was resuscitated in about five minutes by clearing of air passage, tongue traction, alpha-lobelin and carbon dioxide and oxygen. The first placenta which proved to be entirely separate from the second, appeared at the vulva and delivered spontaneously at 9:50 P.M. The bleeding was moderate but steady.

As no uterine contractions were observed and bleeding continued, the second sac was ruptured and the baby, a vertex somewhat larger than the first, was delivered by

version and extraction at 9:55 P.M. The child was in good condition and cried promptly. Following the birth of the second infant, 1 c.c. of obstetric pituitrin was given intramuscularly. The presence of the second placenta seemed to prevent proper contraction of the uterus and complete control of bleeding from the site of the first placenta. Efforts at expression only increased the bleeding and had no effect on the second placenta which apparently had not separated. The uterus was again invaded and the second placenta found firmly attached on the upper right anterior wall, in about the normal position. This was removed intact at 10 P.M. and another cubic centimeter of obstetric pituitrin given with good results, as the uterus promptly shut down, became well contracted and bleeding ceased. The uterus was not packed. The cervix was then drawn down with sponge forceps and, by aid of a speculum, its circumference was carefully examined. There was no evidence of laceration or cervical bleeding but the anterior lip was extremely thick and edematous. The perineum was undamaged. The placentas were of average size, no cotyledons missing, and membranes judged complete. The cords were of average length, inserted centrally and with no knots. The first placenta showed flattening and thinning of the cotyledons along one margin for about 10 cm.; the extreme edge was tough and fibrous; and there were small, dark organized clots in the interstices of the cotyledons.

Postpartum bleeding was slight and the blood pressure immediately after delivery was 120/80 and pulse 88, so that neither transfusion nor infusion was deemed necessary. The first twin, a boy, weighed 3,250 gm. and the second twin, also a boy, 3,750 gm. The next morning, twelve hours following delivery, the patient's red blood cells numbered 3,260,000, and hemoglobin was 70 per cent. Convalescence was uneventful and the puerperium was without morbidity. The temperature did not reach 100.5° F. at any time. Mother and babies were discharged from the hospital on the ninth day, in good condition.

### TUBERCULOSIS AND ADENOMYOMA\*

A. F. LASH, PH.D., M.D., CHICAGO, ILL.

*(From the Gynecological Department of the Mt. Sinai Hospital and the University of Illinois, College of Medicine)*

THE patient, A. L., thirty-seven years of age, entered the Mt. Sinai Hospital July 6, 1931, complaining of menorrhagia of four months' duration. She had lost thirty pounds in the past year. She had had frequency of urination for seven years following a cold and dysuria for about two months, but both symptoms subsided one month before admission following the taking of medication prescribed by her family physician. She had had typhoid fever in 1911 and influenza in 1918. When a child, her abdomen was lacerated as the result of a fall.

Her menses began at thirteen years of age, recurring about every thirty days, lasting three or four days up to the last four months when the duration became ten days. No clots were passed but there was moderate dysmenorrhea. Her last period was June 15, 1931. She had been married eighteen years but had never been pregnant. Her father died of dropsy and her mother died of pleurisy.

Physical examination revealed a well-nourished white female with normal temperature and pulse. Her blood pressure was 165/105. The essential findings were found on bimanual vaginal examination. The corpus uteri was represented by

\*Presented at a meeting of the Chicago Gynecological Society, December 15, 1933.



multiple hard nodules reaching the size of a twelve or fourteen weeks' pregnancy, was upright and free. The adnexa were palpable, not tender. Speculum showed multiple nabothian cysts in an apparently normal nulliparous cervix.

Under the diagnosis of fibroid uteri the patient was prepared for operation on July 8, 1931. An abdominal subtotal hysterectomy, bilateral salpingectomy and right oophorectomy was done. The patient made an uneventful recovery and left the hospital on her twelfth postoperative day.

*Pathologic Report (Dr. I. Davidsohn).*—The specimen consisted of a supravaginally amputated uterus which measured about 7 by 7 by 5 cm. The wall measured up to 2.7 cm. in thickness. There was a subserous fibromyoma measuring about 3 by  $2\frac{1}{2}$  by  $1\frac{1}{2}$  cm. and two intramural fibromyomas, the first measuring about 1.2 by 1.2 cm., the second, measuring about 2 cm., were present at the fundus. A few small cavities 1 to 2 mm. in diameter were present in various parts of the fibromyomas. There was a cavity measuring about 2 mm. in diameter near the lower portion of the uterine body, filled with a greenish material. The myometrium was soft and pinkish white in color. The endometrium was congested, smooth, and showed no evidence of ulcerations.

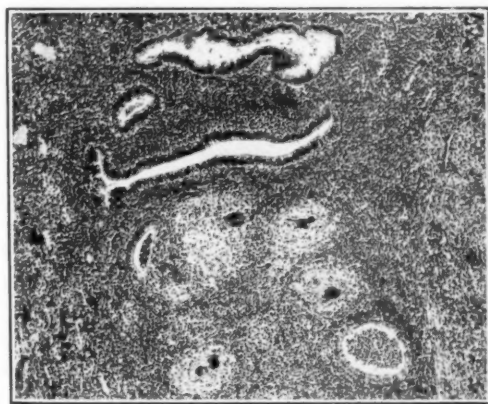


Fig. 1.—Photomicrograph illustrating adenomyoma and tuberculosis of the uterus.

A tube measured 5.5 by 1.5 cm. Its distal portion is thickened. On the cut surface, the mucous membrane was swollen and infiltrated. The lumen was filled with a brownish material. Attached to the distal portion of the tube was a membranous piece of tissue, a part of which appeared quite firm; it measured about 2.3 by 1.7 by 0.3 cm.

*Microscopic Examination.—Endometrium:* The glands were cystically and unevenly dilated. The epithelial cells were crowding each other. In a few places the glands formed adenoma-like structures with papillary projections and rather dark staining epithelium. The stroma was dense in places. In others, it was edematous. There were numerous typical tubercles with lymphoid, endothelioid proliferation, with giant cells and with necrosis. The endothelioid reaction was very prominent. The endometrium showed a marked tendency to penetrate rather deeply into the myometrium and a few of such deep proliferated areas showed tubercles.

*Fibromyomas:* The fibromyomas showed a diffuse, moderate edema and numerous islands of endometrium with glands and stroma.

*Tube:* Some sections of the tube showed complete necrosis and caseation filling out the lumen. In other sections, the mucosa was well preserved but infiltrated with

lymphocytes and plasma cells, and in places there were accumulations of endothelioid cells and of giant cells with peripherally located nuclei.

*Pathologic Diagnosis.*—Tuberculous endometritis and tuberculosis in adenomyosis; hyperplasia of endometrium; multiple adenomyomas with tuberculosis; tuberculous salpingitis (Fig. 1).

One month after operation (August, 1931) the patient was examined for possible tuberculous foci in the chest and urinary tract. No evidence of pathology was found. On Dec. 11, 1933, she was again examined. She had gained in weight and looked well. However, she complained of dysuria and frequency. Cystoscopic examination showed some bullous edema around the right ureteral orifice. Urinalysis revealed the presence of tubercle bacilli.

The interest in this patient is not only the unusual combination of pathologic entities but demonstrates the importance of follow-up in patients who have had a tuberculous focus. The tuberculous process was considered to be an extension of a tuberculous endosalpingitis to the endometrium and then to the adenomyoma.

## SECONDARY LYMPHOGRANULOMATOSIS VULVAE\*

A. F. LASH, PH.D., M.D., CHICAGO, ILL.

(From the Gynecological Department of the Mt. Sinai Hospital and the University of Illinois, College of Medicine)

THE following case of lymphogranulomatosis vulvae secondary to the rectal lesion is interesting in that the histologic picture resembles that of tuberculosis, which was considered the etiologic factor by Huguier in 1848.

B. L., a white woman, thirty-six years of age, entered the Mt. Sinai Hospital on Nov. 13, 1933. She complained of a white leucorrhea and a growth on her left labium minus of from five to six years' duration. The labial lesion had produced pain for the last two years whenever the patient sat down.

A stricture of the rectum necessitated a colostomy eight years ago. Six weeks after the operation the stricture was dilated. Since the stricture allowed normal bowel movements to occur, the colostomy was closed.

She had had a maculopapular eruption around the anus and on the chest, Sept. 3, 1931. She gave the history of having received antisyphilitic therapy for eight years. Her menstrual function was normal. She had been married for eighteen years; she had two children, seventeen and fourteen years of age. She had two induced abortions. Her husband died eight years ago of heart disease and syphilis.

After continued antisyphilitic therapy the Wassermann test became negative on Dec. 14, 1932. Two Frei tests were done in March (29) and April (5), 1933, which were strongly positive. After eight Frei antigen injections the patient's lesion did not improve.

The essential findings on physical examination were: a scar in the right lower quadrant; no palpable inguinal adenopathy; the left labium minus replaced by an ulcerative lesion about 4 by 7 cm., whose edges were grayish white, raised, and hard. The base was firm, irregular, nodular, and grayish yellow. The lesion extended around the fourchette to involve the right labium minus partially. Rectal examination disclosed a hard, sharp obstruction about 2.3 cm. above the anal margin. Posterior to the anus were two small non-discharging, blind sinuses.

\*Presented at the Chicago Gynecological Society, December 15, 1933.

Physical and x-ray examinations of the chest revealed no pathology. Urinalysis revealed no pathologic findings. Blood count: R. B. C. 4,800,000; W. B. C. 5,800; hemoglobin 80 per cent. Wassermann tests were negative.

A diagnosis was made of secondary lymphogranulomatosis vulvae. On Nov. 17, 1933, a simple vulvectomy was done. The lower margin of the wound was open and was covered with a thick yellow exudate when the patient left the hospital the fourteenth postoperative day. The treatment was external irrigations with mild antiseptics, iodoform dusting powder and exposure to the ultraviolet rays.

*Pathologic Report (Dr. I. Davidsohn).*—The specimen consisted of a large, flat mass of tissue representing left labium minus, of a narrow strip representing the right labium and the clitoris. An irregularly shaped, shallow ulcer was present on the left labium, measuring about 2 cm. in the largest diameter. The edges were sloping. The consistency on the base of the ulcer and of the entire surrounding tissue was firm and on the section surface they appeared white. The right labium also appeared thickened and infiltrated.

*Microscopic Examination:* Sections from the ulcer on the left labium showed a thick, leucocytic and fibrinous exudate covering the surface. Underneath, there was a young granulation tissue present with many giant capillaries, fibroblasts, and



Fig. 1.—Photomicrograph illustrating tubercle-like lesion in the labia minora of lymphogranuloma. Giant cells have a more "foamy" appearance than the typical Langhans giant cells of tuberculosis.

some newly formed connective tissue, and in addition, there was present a very dense infiltration with plasma cells and lymphocytes extending deeply into the underlying tissue. Deeper down this change was followed by the presence of nodules consisting of lymphocytes and epithelioid cells and many giant cells with many peripherally located nuclei surrounding a pink staining homogeneous material. These accumulations had the typical morphology of tubercles (Fig. 1). They were present all through the entire thickness of the specimen. Some thickening of the intima of the arteries was also present. The tubercles and a dense infiltration with plasma cells were also present in the areas which were covered with normal appearing, though hypertrophied squamous epithelium. The tissue was very hyperemic. In some places, there was present a necrotic, pink staining tissue in the center of a large tubercle. Sections from the right labium showed the identical changes as were present in the left labium except that the infiltration was less marked, and instead there was present a diffuse serous edema.

Although tuberculosis was considered, in view of the repeated positive Frei tests and anorectal lesions, the diagnosis of lymphogranulomatosis of the elephantiasis, chronic ulcerative type was made.

## TUBERCULOSIS OF THE FALLOPIAN TUBES, UTERUS AND UTERINE CERVIX\*

CHRISTIAN D. HAUCH, M.D., CHICAGO, ILL.

MRS. E. S., aged twenty-three, white, nullipara, was admitted to the Evangelical Hospital, June 14, 1932. Her chief complaints were odorous vaginal discharge, irregular, painful menstruation, metrorrhagia, and pain and tenderness in the lower abdomen. The symptoms varied in severity from time to time, but had persisted for eight years. There was a history of a severe influenzal infection at the age of ten. Four years later the patient was in a sanatorium for eight months for pulmonary tuberculosis. Menstruation began during her sixteenth year. At times the flow was continuous for weeks; then again there were intervals of amenorrhea for several months. There was no history of pregnancy during eight years of married life. In October, 1931, a diagnosis of acute salpingitis was made, but it could not be classified as gonorrheal from the history nor from the laboratory findings. The acute symptoms subsided in a few days, but the vaginal bleeding and discharge persisted. During the years of impaired health the patient's appetite was usually good and she maintained a weight of about 120 pounds which was average for her height.

On admission to the hospital the pulse, temperature, and respiration were normal. Abdominal tenderness and rigidity were limited to the lower quadrants. The uterine cervix was enlarged and hard, and the portio vaginalis was studded with a few pea-sized papules with ulcerated apices which bled on manipulation. The uterus was slightly enlarged, hard, retroverted, and fixed. The adnexa were tender on palpation, nodular, fixed, and enlarged to twice normal size.

The urinary findings were normal. The blood Wassermann reaction was negative. Hemoglobin was 80, red cell count 4,300,000, and white cell count 9,700. One differential cell count showed 37 per cent lymphocytes. The x-ray examination of the chest revealed a few calcified lymph glands in each hilum. There was one large gland in the left hilum which was probably tuberculous. There were no evidences of active tuberculosis in the parenchyma of the lungs. The pleura was normal. The pathologist reported positive tubercular changes in cervical and endocervical tissues removed for diagnostic examination.

On June 16 a panhysterectomy was performed which confirmed the clinical findings in the pelvis. Dense adhesions were encountered, but no tubercles were found on the peritoneal surface anywhere. There was very little free fluid in the peritoneal cavity. The abdomen was closed without drainage.

Except for surgical shock continuing about seventy-two hours the postoperative course was without complications. The patient was discharged from the hospital on July 2. She has since gained twenty pounds and feels very well. There is still a slight vaginal discharge, but no apparent ulceration nor bleeding.

The gross specimen showed definite caseation within the tubes, and ulceration on the vaginal portion of the cervix. Tubercles, giant cells and tubercle bacilli are demonstrable in the cervical, endocervical, and endometrial tissues. Tubercles and giant cells are also present in the tubal and myometrial structures.

6200 SOUTH TROY STREET

\*Presented at a meeting of the Chicago Gynecological Society, December 15, 1933.

## TUBERCULOUS SALPINGITIS DISCOVERED INCIDENTAL TO SALPINGOSTOMY\*

DR. ARTHUR B. HUNT, CHICAGO, ILL.

THE patient, a twenty-seven-year-old nulligravida, entered the gynecology clinic of the Lying-in Hospital Out-Patient Department, Feb. 4, 1931. The only complaint was sterility during the six years of her married life.

She had had typhoid fever as a girl. The menses were established normally at fifteen, regular every twenty-eight days, with moderate flow of three days' duration; no clots or dysmenorrhea. A premenstrual leucorrhea had occasionally been present. The weight had remained constant, about 127 pounds.

The only positive findings were the presence of enlarged cryptic tonsils and an accessory nipple of the right breast. There was some thickening and tenderness of both adnexa on pelvic examination. A Rubin's insufflation test and lipiodol injection in February, 1931, revealed: gross dilatation of fallopian canals in their distal portions on both sides and the fimbriated end of the right fallopian tube located high in the abdomen over the curve of the right iliac bone where the appendix is usually found. It was impossible to state absolutely whether the fallopian canals were patent, though probably the left was open.

The preoperative diagnosis was chronic bilateral salpingitis and chronic tonsillitis.

At laparotomy Sept. 24, 1931, both tubes were found to be tortuous, enlarged and closed at the fimbria. There were small cystlike bodies  $\frac{1}{2}$  cm. in diameter on the upper surface on the left tube 3 cm. from the cornua which were thought on gross inspection to be cysts of Morgagni. The left ovary contained a simple follicle cyst 3 to 4 cm. in diameter. The right ovary also contained a few very small follicle cysts. The appendix was long, tortuous, hyperemic, and bound down by adhesions. An appendectomy was done.

On the fourteenth postoperative day a lipiodol injection showed perfectly normal patency of the right fallopian canal with lipiodol free in the right side of the pelvic cavity. Patency of the left tube was doubted. The patient received two subsequent tubal insufflations with patency demonstrated.

On microscopic examination both tubal fimbriae showed the plicae thickened and adherent to one another forming many glandular appearing spaces all lined by a single layer of columnar epithelium with no abnormal tendency toward proliferation. There were areas of cellular infiltration where plasma cells and small lymphocytes predominated but where numerous epithelial cells were also present. Tiny areas of necrosis were seen. One slide showed many atypical giant cells and in some cases necrosis but no typical tubercles were present. There was an old inflammatory process in the appendix, nontuberculous.

The diagnosis was tuberculous salpingitis.

No evidence of any active tuberculous focus could be demonstrated elsewhere on subsequent examination of the patient.

Temperature readings four times a day, for two weeks, on two different occasions showed not a single febrile reading. However, the patient was placed on a lenient

\*Presented at a meeting, December 15, 1933, of the Chicago Gynecological Society.



tuberculosis regime for several months with some weight gain and her general health continued to be excellent.

No pregnancies have resulted from the salpingostomy.

This case shows strikingly the value of routine pathologic examination of all tissue removed at operation. It also raises the possibility that all cases may not merit strenuous efforts to establish fertility because of medical or other complications.

### MICROSCOPIC VISUALIZATION OF THE CERVIX UTERI

HERBERT A. SACKS, M.D., CHICAGO, ILL.

THE object of this paper is to present an original method of colposcopy, which does not require expensive instruments and has a simple technic; and one it is hoped will come into universal use.

The early diagnosis of cancerous lesions of the cervix uteri is very important from the clinical point of view. It is only by the early recognition and proper treatment of precancerous conditions, that the mortality of cervical malignancy will be reduced. The discovery of small erosions,

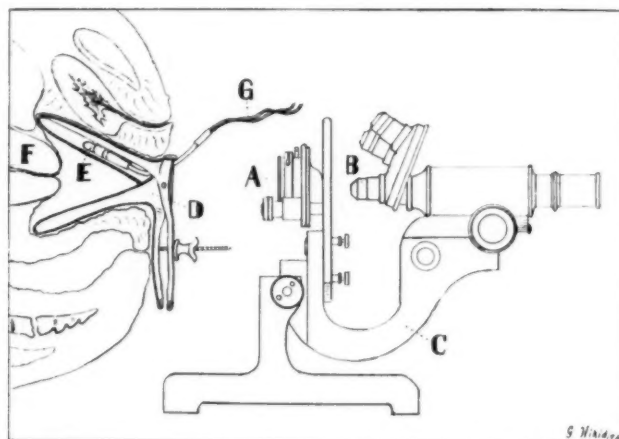


Fig. 1.—Microscopic cervical visualization. A, Abbe condenser; B, 10 x objective; C, microscope; D, vaginal speculum; E, miniature bulb; F, cervix; G, cords to battery or transformer.

leucoplakia, ectropion, and small nodule formations is a great step forward in this direction. The difficulty is that early changes frequently are overlooked by the ordinary visual speculum examination, because these lesions may be very minute and not visible to the naked eye.

Instruments have been devised to produce a magnification of the cervix and to aid the discovery of these early changes, such as leucoplakia and nodule formation. The colposcope was introduced by Professor Hinselmann of Hamburg with this aim in view, and consists of a binocular endoscope which enlarges the cervix from three to thirty times. This instrument has been used by E. Ries and W. Schiller and has been stated to be a definite aid in the differentiation and diagnosis of cervical pathology.

Stoeckel in his *Handbook of Gynecology* presents many instructive illustrations of early changes in the cervix as revealed by the colposcope.

A modification of this instrument has been made by Cameron, which uses a monocular telescope instead of the cumbersome binocular endoscope of Hinselmann and has been described by R. Lifvendahl. The main objection to all of these instruments is that they are costly, which has prevented them from becoming a routine procedure in all gynecologic examinations.

The principle of the suggested method of colposcopy which we shall call "microscopic cervical visualization" consists in the use of the substage, i.e., Abbe condenser of the ordinary clinical microscope as a telescopic lens, with illumination of the cervix by a miniature electric bulb fixed to the vaginal speculum; to produce an upright magnified image of the cervix to the eye of the observer.

The technic of this method in detail is as follows: A vaginal speculum (*D*) with black plated blades on the inner surface to decrease light reflection, is inserted in the vagina, and a two and a half volt miniature bulb (*E*) is fastened by a metal clip to the inner side of the anterior blade of the speculum about two and a half inches from the end. This bulb is lighted by a battery or transformer from an electrical outlet (*G*). The cervix (*F*) is carefully dried of any secretion and the microscope (*C*) is tilted to a horizontal position and the mirror is removed. The substage condenser (*A*) is placed about six inches from the speculum opening and at the same level with it. The ten power objective (16 mm.) is next turned into place, and focus is made with the coarse adjustment until the cervix (*F*) comes into view. The five or six power eyepiece should be used in place of the ten power lens as it gives a larger field and less distortion of the image. Lowering and raising the speculum will give a clear field of the entire cervix to the examiner. Examination in a dark room will help cut obstructive rays of light and give a better contrast to the magnified image.

A method of cervical visualization using the substage condenser of the microscope as a telescopic lens is described in detail. This method should come into routine use in all gynecologic examinations of women at the carcinoma age.

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1608 WEST MADISON STREET

## BANTI'S DISEASE COMPLICATING THE PUERPERIUM\*

DOROTHY L. ASHTON, A.B., M.D., PHILADELPHIA, PA.

(From the Department of Gynecology, Women's Hospital of Philadelphia)

A WHITE primipara, aged twenty-five years, whose history showed nothing abnormal except a moderate anemia, had after a labor of ten and three-quarters hours and delivery by low forceps, a profuse hemorrhage from the uterus which required packing.

On the fourth day postpartum, the patient's temperature rose to 101° F. The spleen was found unexpectedly palpable below the rib margin; hemoglobin was 34; R.B.C., 1,670,000; W.B.C., 5,900. Three transfusions were given at three-day intervals. During this time the temperature rose to 104° F. on several occasions, and the spleen persistently increased in size until it reached slightly below the level of the umbilicus. The platelet count was 190,000; the coagulation time, two and one-half minutes, the blood Wassermann, negative. Tests for typhoid, paratyphoid, and malaria were consistently negative, and the blood culture showed no growth. On discharge on the twenty-eighth day, the blood count read: Hb. 36; R.B.C., 2,020,000; and W.B.C., 2,300. The spleen, slightly smaller than its greatest size, still reached to the umbilicus.

For five months the patient lived at home, did her own housework, and felt moderately well, except for easy fatigue and palpitation on exertion. At the end of this time, her blood count read as follows: Hb. 60; R.B.C., 4,000,000; W.B.C., 2,000; reticulated reds, 3.2 per cent. The red cells showed considerable anisocytosis, poikilocytosis, and very slight polychromatophilia. On the basis of these findings, the clinical history, and the size of the spleen, the diagnosis of Banti's disease was made and splenectomy was advised as the only procedure offering permanent improvement. Accordingly, the patient was admitted to the Women's Hospital for operation. At this time there was elicited from her a history of frequent scanty nosebleeds since grammar school age, and an acute illness four years before her pregnancy, which lasted about four weeks and resembled typhoid fever, but showed no rash. The symptoms of this illness included diarrhea, nosebleeds and frequent headaches. Following this she had an amenorrhea until her marriage when her periods gradually became regular.

When she was admitted to the Women's Hospital on Feb. 13, 1931, the liver was not palpable; the spleen extended from an area two fingerbreadths below the costal margin on the left, across the abdomen on a level with the umbilicus to an area two fingerbreadths beyond the midline. The icteric index was 53.4, direct van den Bergh diphasic, and indirect van den Bergh 9.1 units. Following a blood transfusion of 500 c.c., splenectomy was performed on Feb. 27, 1931. The spleen was found to be densely and universally adherent to the parietal peritoneum.

*Pathologic Report.*—The spleen measured 24 by 14 cm., but preserved a normal shape. The capsule was moderately thickened, the substance soft, but not friable. Microscopically the sinuses were greatly enlarged, and their walls showed the increase in fibrous tissue typical of Banti's disease.

\*Read at the meeting of the Obstetrical Society of Philadelphia, Dec. 7, 1933.

The patient's condition on the operating table was fairly good. Postoperatively, however, there was a rise of temperature, a rise of the white blood count to 28,000, and alarming bleeding each time any effort was made to move the packs. She died March 30, 1931, thirty-three days after operation, of hemorrhage, on an attempted removal of abdominal packing.

Autopsy, which was limited to abdominal examination, revealed gauze packing firmly adherent to omentum, diaphragm, and pancreas,  $\frac{1}{2}$  liter of comparatively recent blood clots in the area from which the spleen had been removed. Two liters of clear amber-colored fluid were found in the abdominal cavity. The stomach contained coffee-ground material, and its walls showed petechial hemorrhages. The intestines appeared normal. The liver was small, firm, hobnailed, and mottled gray and green.

### ACUTE THYROIDITIS COMPLICATING THE PUERPERIUM

PHILIP B. WAHRSINGER, M.D., NEW YORK, N. Y.

*(From the Obstetrics Service of The Bronx Hospital)*

ACUTE thyroiditis is a very rare condition. Dr. H. M. Richter reported two cases in a series of over 2,000 goiter patients. In the Lahey Clinic it was seen three times in over 3,000 thyroid operations. An exception is made to the rarity of this condition by Mora<sup>1</sup> who from 1921 to 1928 reports 6 cases from the Cook County Hospital where the amount of goiter material is comparatively small. Another exception is Hagenbuch who found 43 cases among 45,953 medical and surgical admissions to the Basle Clinic during a ten-year period.

Mrs. R. Z., forty-year-old female, gravida iv, para i was observed in the Prenatal Clinic of The Bronx Hospital. Physical examination was negative except for an old scar in the right lower quadrant of the abdomen from a previous operation for right ovarian cyst. She was delivered at term by low forceps because of uterine inertia, the head being on the perineum for one hour, and maternal exhaustion. There was a small first-degree laceration which was repaired with one chronic catgut suture.

On the seventh day postpartum the temperature rose to 101.2° F. There was tenderness in the left iliac region and an indurated mass extending almost to the pelvic brim. There was also definite cystic, tender enlargement of the right lobe of the thyroid.

On the eighth day postpartum, the swelling in the right side of the neck was distinctly smaller. The left lower abdominal mass was still present and tender. Temperature was 100.8° F. The patient's condition remained unchanged, temperature ranging between 98.6° and 101° F. until the twelfth day when the temperature rose to 101.4° F. At this time the mass in the neck had not changed in character, but the mass in the left iliac region was smaller in size and less sensitive. On the following day the temperature was 102° F. and the patient complained of pain on swallowing and more intense pain in the right side of the neck. The right lobe of the thyroid appeared larger and tenderness had increased. The abdominal mass was considerably smaller.

Tracheoscopy done revealed no evidence of pressure. The mucous membrane of the trachea was somewhat congested. There was slight fullness in the right pyriform fossa. Blood count showed 11,000 leucocytes, with 81 per cent polymorphonuclears. The thyroid continued to increase in size the next day, and it was also

noted that the pupils were unequal in size, the right being larger and reacting more sluggishly to light.

Vaginal examination failed to reveal a definite exudate although the uterus was very much enlarged and subinvolved. Lochia was not foul. Blood count now showed 15,000 W.B.C. and 78 per cent polymorphonuclears. Further increase in the size of the mass in the neck and deviation of the larynx and trachea to the left were noted on the sixteenth day postpartum. The voice was husky and while this may have been the effect of the laryngoscopy, it may also have been due to pressure. The mass previously felt in the left iliac region could no longer be felt. Surgical consultation at this time reported: "Mass in the region of the right lobe of the thyroid has increased in size and is more tender than when seen before. Impression is that of a thyroiditis due to metastatic infection possibly from the pelvis. It appears as if suppuration is developing in the middle of the mass." The huskiness of the voice disappeared three days after its onset. The mass diminished in size although the trachea and larynx were still deviated to the left. On the twentieth day postpartum the mass was about half its largest size and it was no longer tender. Patient was discharged on the twenty-third day with some enlargement of the right lobe of the thyroid. She was advised to return for removal of thyroid nodule four to six weeks postpartum.

A basal metabolism a day before discharge showed a reading of plus nine.

Patient was seen six weeks postpartum in the clinic and slight enlargement of the right lobe of the thyroid was found to be present. No tenderness was found on palpation. Uterus was normal in size, and there was no evidence of pelvic exudate.

It is interesting to note that the above case is the only one found in approximately 4,800 deliveries at The Bronx Hospital since January, 1927.

1229 CLAY AVENUE

## LITHOPEDION

C. GORDON JOHNSON, M.D., AND SEWARD H. WILLS, M.D.,  
NEW ORLEANS, LA.

(From Charity Hospital, Department of Gynecology, Tulane University)

A J., colored female, aged forty years, was admitted to Charity Hospital July 17, 1933, with a tentative diagnosis of multiple uterine fibroids. Her chief complaint was pain in the lower abdomen and in the lower midsacral region. About seven years ago she had experienced a rather acute onset of pain in the lower abdomen, especially on the right side, this attack forced her to remain in bed for about two weeks. She does not remember whether she had missed any menstrual period prior to the onset of this attack, or if there was any vaginal bleeding during this attack. Since that attack she has complained of a continuous dull pain in the lower abdomen and in the midsacral region. During the past month these pains have increased in severity to such an extent that she has been confined to bed for two weeks prior to admission. During this seven-year period there has been a feeling of heaviness in the lower abdomen; also a constant desire to urinate, following which there is some relief from the pain. Bowel function is apparently normal.

The past history is of no particular significance, there being the usual diseases of childhood. There have been no previous operations.

Menstruation began at sixteen years, has been regular, occurring every twenty-eight to thirty days and lasting from five to seven days. The L.M.P. began July



4, lasting to July 10, 1933. There have been 3 pregnancies, the oldest child being twenty, the youngest being twelve.

The patient was a middle-aged colored woman, not acutely ill. There was a palpable hard mass in the lower abdomen, most prominent on the right side, movable and tender on deep palpation.

The uterus appeared to be about the size of a four months' pregnancy, rather firm and irregular; the adnexa apparently normal.

The preoperative diagnosis was uterine fibroids and chronic bilateral salpingitis, the postoperative diagnosis was lithopedian, and chronic bilateral salpingitis.

Under ether anesthesia the abdomen was opened in the midline below the umbilicus. A hard calcified mass about the size of a five months' pregnancy was found completely surrounded by the greater omentum. This mass was lying anterior to the uterus, which was of normal size. The mass was removed without difficulty, and was found to be a calcified fetus. The right tube was found to contain at its fimbriated end a calcified mass about the size of a walnut; this apparently being the original site of the placenta. The left tube was found to be chronically diseased, the lumen being closed at the fimbriated end. There was a small cyst of the left ovary, which was punctured. The remaining ovarian tissue was apparently in good condition. A bilateral salpingectomy was then done, and a right oophorectomy was also performed because of persistent bleeding from this ovary. The abdomen was closed in anatomical layers.

The specimen consisted of a tube and a fetus. The fetus measured approximately 18 cm. in length. One arm of the fetus had been amputated apparently due to the operation. Examination of the fetus disclosed it to be entirely calcified. The original appearance had been well preserved. It was evidently a lithopedian. On sections the stony wall measured 3 cm. in diameter, and contained a thick yellow creamy material which had no odor. No sections made, it being preserved as a museum specimen.

The postoperative course was somewhat prolonged because of the development of a wound infection, recovery, however, being complete.

This case is apparently one of a right tubal pregnancy which terminated in a tubal abortion. The pregnancy then continued as an abdominal one for approximately four to five months, at which time fetal death occurred and calcification of both the fetus and the placenta took place. It is of interest further because of the fact that the original features of the fetus were very well preserved.

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**Werner, E.: The General Treatment of Leukorrhea, Monatschr. f. Geburtsh. u. Gynäk. 94: 166, 1933.**

The most effective way of overcoming leucorrheal discharges is local treatment. However, better results will be obtained if, in addition, general treatment is instituted. A vegetarian diet has a favorable effect on the entire body because of its stimulating effect and its influence in preventing inflammation. Calcium and vitamin D markedly support these effects. Natural or artificial sunlight is also highly beneficial.

J. P. GREENHILL.

## RUPTURED UTERUS FOLLOWING CLASSICAL CESAREAN SECTION WITH A NORMAL BIRTH DURING THE INTERVAL

PHILIP V. FAVA, M.D., NEWARK, N. J.

MRS. M. P., para ii, aged twenty-eight, white, was operated upon in 1922. A classical cesarean section was done, the indication being beginning eclampsia. A living male child was born Sept. 29, 1922. She was discharged on October 15. On May 6, 1926, she delivered a living male child normally. She was discharged on May 16.

In April, 1932, she was operated upon by me for postoperative adhesions and at the same time her appendix was removed and a small cyst of the right ovary was resected. She was discharged on May 1. Since this time she had remained in good health up to the month of June, 1933. At this time she was about five months pregnant, her blood pressure was 110/80 and the urine negative. Her last menstrual period was said to have occurred on Jan. 24, 1933. On the twenty-third of September, 1933, approximately one month prior to her estimated date of delivery, the patient began to have pains about midnight. A vaginal examination was made, the head was found partially engaged and the cervix about two fingers dilated. The temperature at this time was normal and her pulse of good quality. Her abdomen was soft and the fetal parts could easily be palpated and the fetal heart heard. Shortly after midnight she vomited a few times, to which no significance was given. Early Sunday morning at about 8 o'clock the pains became somewhat more severe and the vomiting still persisted. At this time her temperature and respirations were still normal but the pulse was somewhat quickened. No vaginal examination was made at this time, the pains had begun to be less severe, and there was no appreciable progress. The fetal heart tones were still audible. At eleven o'clock this same evening the patient suddenly went into profound shock, the pulse was now imperceptible and the temperature subnormal. The abdomen was markedly distended, rigid, and tender throughout. A peculiar bluish discoloration was visible throughout the entire thin abdominal wall. A diagnosis of ruptured uterus was made and the patient immediately moved to the hospital where a supravaginal hysterectomy was done.

The operation itself revealed many adhesions, the fetus being found in the upper abdomen and the uterus in the lower abdomen poorly contracted. The abdomen was filled with blood but the amount was not estimated. On inspecting the uterus after it had been removed, a tear was found in the site of the old classical cesarean scar. This tear seemed to have begun in the lower uterine segment and extended throughout the entire body of the uterus.

The operation was done under ether anesthesia during which the patient ceased to breathe as the abdomen was being closed.

This case is identical with that of Edward L. Cornell of Chicago, Ill., who reported his case in the August, 1929, issue of this JOURNAL.

220 SOUTH SEVENTH STREET

## SECONDARY ABDOMINAL PREGNANCY

EARL C. SAGE, M.D., AND C. R. KENNEDY, M.D., OMAHA, NEB.

MRS. W. H. E., a primipara, aged thirty-five years, first consulted me Jan. 30, 1933. Her last menstrual period was October 26, 1932. She complained of soreness across the lower abdomen, of pain while defecating, and of occasional cramps. Vaginal examination showed she was very tender—the recti muscles were quite tense, but it was my impression that she had a retrodisplaced pregnant uterus. She was advised to take knee-chest exercises and told that it might be necessary to examine her under anesthesia and raise the uterus.

On Feb. 3, 1933, she complained of pain in the epigastrium. Her abdomen was quite distended. She attributed her discomfort to the fact that the night before her husband had playfully dropped their 16-pound bull dog on her stomach while she was lying on the davenport. She said she was too tender to allow any examination; she looked ill, and appeared anemic. She was urged to enter the hospital. Her husband was at home intoxicated, and the patient refused to leave him. The husband's fondness for alcohol must be included in the history because of subsequent events. This inebriety at a later crucial time markedly complicated matters as to treatment. At this time repeated enemas relieved the wife's abdominal distention, and she felt well the following day.

She returned to the office Feb. 13, 1933, and vaginal examination showed the uterus retrodisplaced and seemingly part of the mass which could be felt above the symphysis, but still the examination was unsatisfactory because of tenderness and rigidity of the abdominal muscles.

Because of crampy pains in the lower abdomen, she entered the Methodist Hospital four days later, Feb. 17, 1933, and was examined under gas anesthesia. The uterus was lifted up and seemed incorporated with the mass in the lower abdomen. The red blood count was 3,570,000; white blood count, 17,500; hemoglobin, 65 per cent; differential count 85 per cent polymorphonuclears, 15 per cent lymphocytes. The temperature was 99.2° F. She was upset mentally about her husband, who had continued drinking and who insisted on visiting her at the hospital while he was quite intoxicated. Two days later the husband became so wobbly that he was put to bed in the hospital where he stayed for three days. (February 19, 20, and 21.)

During this time Mrs. E. became more nervous, had cramps in the lower abdomen, complained of more pain, and required opiates for relief. The abdominal distention became more marked and was not relieved by the ordinary methods, enemas and stomach lavage.

On February 20, the patient was advised to have an abdominal operation, but she refused that night hoping that her husband would be responsible the next day and give her the opportunity to talk the matter over with him. He left the hospital that morning and was drunk again in the afternoon.

On February 21, after consultation, immediate operation was undertaken as a life-saving measure. That morning the patient had a little bloody vaginal discharge; the cervix was one finger dilated, and a piece of what looked like placenta was expelled. This, of course, was a decidua cast.

Operation: A midline incision was made through the distended abdominal wall into the peritoneal cavity. Immediately presenting was a loop of large bowel

immensely distended easily measuring 4 in. in diameter. Below this toward the pelvic cavity, was a walled-off sac, the wall of which was the right broad ligament, which had ruptured allowing the escape of a 16.5 cm. fetus, perfectly formed. Organized clots of blood were present, and this together with the placental tissue was removed without any attendant hemorrhage. This material weighed 332 gm.; the fetus weighed 140 gm., in the fourth month of development. The uterus was felt in the pelvis, being pushed backward.

An enterostomy was performed to relieve the bowel obstruction by sewing in a large rubber tube, and Penrose drains were put down into the bottom of the sac formed by the right broad ligament. Routine closure of abdomen, with absorbable and silk-worm-gut sutures.

The patient had a very stormy postoperative course. Her temperature rose to 104.2° F.; she received a blood transfusion on the fourth postoperative day; her temperature ranged from 99°-102.6° F. for the next two weeks.

A fecal fistula was evident on the eighth day and on the tenth day the colostomy tube was removed; a large amount of fecal matter was evacuated through both these openings.

On the thirty-ninth day (April) she was sent home to see if this fistula would close. The opening into the bowel became appreciably smaller, and she had a good many normal stools through the rectum, but the fistula persisted; on August 4, she entered the University of Nebraska Hospital. On Aug. 7, 1933, Dr. C. R. Kennedy repaired the bowel wall. This fistula was in the sigmoid flexure of the colon where probably part of the placental growth had attached itself. She made an uneventful recovery, being discharged on her twelfth postoperative day. Her wound healed perfectly, and there were no complications. She had a slight elevation of temperature, 101.4° F. for the first three days.

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**Benedict, W. L.: The Relation of Infection of the Pelvic Organs and Diseases of the Eye, Wisconsin M. J. 32: 85, 1933.**

In a former paper the author called attention to the connection between infection of the cervix and recurrent scleritis of women in which evidence of tuberculosis could not be found, and to the improvement of the condition of the eyes following the administration of the autogenous vaccine made from bacteria isolated from eroded cervices. Subsequent observations have repeatedly shown improvement in the inflammation of the eye, following eradication of foci of infection, with particular reference to infection of the cervix and endometrium. The infecting organism was found on repeated cultures to be a strain of green-producing streptococcus. The organism has not been found at all times but repeated cultures have been necessary in some cases, to obtain growth of streptococci from which a satisfactory vaccine could be made. The administration of vaccine is undoubtedly of considerable value for relief of acute inflammation. Intramuscular injections of milk or, after the first or second injection of milk, intravenous injections of typhoid vaccine have been found to be quite effective. The pain subsides and the lesion of the eye begins to fade. Continued observation of these patients has shown conclusively that the eradication of pelvic infection is necessary before complete subsidence of scleritis can be expected.

J. THORNWELL WITHERSPOON.

## Special Article

### JAMES PLATT WHITE AND DEMONSTRATIVE MIDWIFERY\*

HERBERT THOMS, M.D., NEW HAVEN, CONN.

IN THE year 1850 at Buffalo, New York, the trial of *The People versus Dr. Horatio N. Loomis*<sup>1</sup> took place. Although the details of that court action appear somewhat ridiculous to our generation, yet the event is an important landmark in the history of clinical teaching in America. It was this trial and the events leading up to it which began a nation-wide controversy concerning the teaching of clinical obstetrics and which culminated in complete victory for its champion Dr. James Platt White of Buffalo. However, before speaking further of White and his wide influence on American obstetrics it will profit us to study somewhat into the history of the trial we have referred to.

On January 18, 1850, James P. White then Professor of Midwifery in the newly formed University of Buffalo delivered a certain Mary Watson before some members of the senior class of that institution. It was her second child; she was twenty-six years old at the time and was not married. Previous to her confinement she lived for a time with the janitor and his wife at the Medical College, and we find that after the event Dr. White presented her with ten dollars which she averred was no inducement for her to go there. We are informed that the presentation was "occiput to the right posteriorly, face left anteriorly,"<sup>7</sup> and that this position was diagnosed by Dr. White by abdominal examination and furthermore that both before and during labor the students had opportunity to examine the patient. It is a fact also that at no time was the patient unduly exposed and that she was very carefully draped during the labor. In fact, the testimony shows that the whole procedure was carried out with much the same decorum and manner that obtains in similar clinical teaching today.

This was the beginning of the drama of which we can tell but a few details, but that it can be called such is witnessed not only by the extraordinary mass of historical material which has come down to us concerning the event, but more particularly by some of the interesting facts therein. Following this prologue of the confinement of Mary Watson the first act begins with the publication of certain resolutions adopted January 21, 1850, by the candidates for graduation from the Buffalo Medical College.<sup>2</sup> The second of these resolutions stated, "That we feel no ordinary degree of pride and congratulation, in claiming for the Medical Department of the University of Buffalo the honor of being the first, and at present, the only among the American Schools of Medicine, where Clinical Instruction in Midwifery is rendered within the walls of the institution."<sup>7</sup> It was one month later that an editorial<sup>3</sup> appeared in the *Buffalo Commercial Advertiser* said to have been "written avowedly to quiet public excitement by assuring the numerous readers of that most

\*This is one of a series of historical articles which should prove of interest to the reader as a departure from purely scientific contributions.



respectable print, that the editor had examined into the facts and that there was no occasion for any popular dissatisfaction with the demonstration at the College." However, one of the principals in this story who signed himself "L" disagreed most vehemently with this sentiment, and in a rejoinder published in the *Buffalo Daily Courier*<sup>4</sup> of February 22, 1850, he stated his disapproval by such invective as, "A writer in the *Commercial Advertiser*, of this city, has attempted to defend a gross outrage upon public decency, and I claim the right to reply to him, although the subject is one of so delicate a nature as hardly be susceptible of much handling. . . . An open demonstration of obstetrical practice has been made, before a class of students. The demonstration consumed nearly or quite *eight hours* during a part, at least, of which the professor of that branch of medical instruction was present. Delicacy forbids me to touch upon the manner in which those hours were passed—suffice it to say that the tedium was relieved by such methods as a congregation of *boys* would know well how to employ. . . . I look upon the whole thing as an attempt to build up, for *some one*, a reputation, on a basis entirely unworthy the sacred cause of science. The patient was a woman in humble circumstances whose poverty, perhaps, overruled her natural modesty. What mattered it then, if a score of scarcely adolescent youth satisfied their *meretricious curiosity* at her expense? The professor had enjoyed his 'clinique' and his class their *salacious stare* and, under the specious plea of scientific advancement, a precedent had been set, for outrage indiscriminate."

"L" apparently had some members of the medical profession as supporters for seventeen of them wrote to the *Buffalo Medical Journal*<sup>5</sup> (March, 1850) "deeming it (demonstrative midwifery) wholly unnecessary for the purpose of teaching, unprofessional in manner, and grossly offensive." Just before this, however, the defendant at the trial, Dr. Horatio N. Loomis, appeared on the scene and, according to the testimony of W. A. Seaver, editor of the *Buffalo Courier*, came to his office looking for extra copies of "L's" article.<sup>1</sup> However, the type had been distributed and there were no extra copies. This did not daunt Loomis, however, for Attorney Smith's argument in the trial<sup>1</sup> tells us, "One would suppose that the circulation of eight hundred copies of this scurrilous libel would have satisfied the defendant (Loomis). Not at all. He panted for the malignant gratification of circulating it, with his own hand! He contracts with the editor to rent the type—to print another edition—that he will pay for fifty copies of the paper. This is done. The fifty copies are taken away by the defendant, or some one for him—another fifty copies are taken and paid for by some one else—and the libel is republished in the weekly courier, and eight hundred copies more are sent on their errand of malignity and mischief through all the towns of this county . . . armed with an abundant supply of this ammunition of falsehood—the defendant, in his drives and perambulations through the city, keeps a watchful look-out for those of his patients who are *fortunate enough to be abroad*." (Italics mine.) And so by this busy exercise Dr. Horatio N. Loomis obtained for himself the rôle of defendant in the libel action referred to. Although this presents probably a veritable picture of the meddling Loomis, in spite of its extravagant verbiage it is but simple language compared to some of that indulged in, in this interesting record of court procedure. However, it may be well to remember that these were the days when such legal verbosity had been very much set in fashion by the magnificent thunderings of Daniel Webster and his notable contemporaries, and as we look back to that day of tall hats and frock coats, it perhaps does not seem very much out of place. Listen to the defense attorney, J. O. Putnam, Esq., "Dr. White may for aught I know, the modern Prometheus, who has brought down the fire from the gods, with which to illumine our hitherto darkness, and it was left for him to successfully override the usages

of ages, and the prejudices and principles rooted and grounded in us from childhood to old age; yet we shall insist here, that something is to be pardoned to public prejudices, we shall deny his right to stretch us out upon his Procrustean bed, and hack off our limbs, if too long, or stretch them out, if too short, without waiting for us to grow up, or to grow down, to his 'innovating position.' He having thrown down the glove of controversy we shall insist on our right to take it up, and deny that all the discussion is to be on his side. He had had his Eulogium—his innovation, its panegyric. . . . The exposure of this woman in labor, we shall show, substantially as alleged. We shall show you that it was not only a startling and bestial innovation, but without a particle of utility. To the stethoscopical examination we make no objections; against the exposure of this woman whom though the virtuous angels had abandoned, society had not, we do protest." And so proceeds the record of the trial, page after page, the examination of witnesses, the arguments of the prosecution and the defense, the judge's charge, all designated to impress, convince, and, I suspect, to wear down that body of men sitting in the jury box. At all events after several days a verdict was rendered "Not Guilty," for it was not proved that the busybody Loomis had written the article after all. In fact one George Haskins swore that he was the author and that he simply used the letter "L" as his signature. Strange coincidence indeed. With the end of the trial, however, the drama by no means ended, for the interest in the subject among the medical profession became nation wide.

One of the most interesting of the reverberations of the trial was that echoed by Dr. Caspar Morris of Philadelphia, who has been described as "physician, hospital administrator, and poet."<sup>6</sup> In the *American Journal of Medical Sciences*<sup>7</sup> he wrote, "Some of our medical colleges resorted to efforts to allure classes by specious exhibitions *misnamed* 'clinical instruction' and adapted rather to attract students by their novelty than to furnish them with solid information . . . when however, we came to be apprised that the improvement consisted in subjecting the process of parturition to ocular inspection in one of its stages, our surprise at the excitement yielded to astonishment that any teacher of the obstetric art should suppose that it could be made the subject of the sense of vision, and mortification that the medical profession should have been placed in a position so well calculated to array public feeling in hostility to it." White's management of the occipitoposterior position was also assailed by Morris who continues . . . "however, *one great error* appears to have been committed in this stage of the procedure. We were taught by one esteemed through the civilized world as no second rate master of his art, that such a presentation is faulty, and should be remedied in the *early* stage by bringing the occiput into such a position as would permit it to emerge under the arch of the pelvis, while the face followed the curvature of the sacrum . . . we protest against every stage of the proceeding, and shall presently endeavor to justify our objections." It is true that medical authorities were divided in their treatment of posterior position at that time and that Denman and Dewees favored interference while Naegle and other authorities did not. White replied to Morris denying that he made any "discovery" in using the stethoscope to diagnose fetal position and that he was unjustly accused of committing a great error in allowing the labor to go on with the head of the child presenting in the posterior position. Nevertheless, the editor of the *American Journal of Medical Sciences* agreed with Morris and wrote, "We have yet to meet a respectable physician in Philadelphia who does not concur with it."<sup>8</sup>

Most of the sentiment among medical writers was of an opposite nature, and we find such opinions as, "We strongly suspect that the objection to these experiments springs from some of those opposition factions, so commonly found surrounding and

impeding medical schools." (*Cincinnati Medical Journal*, May, 1850), "practical clinical teaching will, ultimately triumph over those who oppose it as alike 'grossly offensively to morality and common decency'" (*New Orleans Medical Journal*, May, 1850). "It is the motive with which he acts that is to be his defense; and if this defense will not avail demonstrative midwifery, neither will it avail the use of the speculum, the attendance of a male obstetrician, or in fact any prescribing by a man for the sexual diseases of females. All must stand or fall together" (*New York Medical Gazette*, July 6, 1850). Anent the seventeen members of the Buffalo Medical Profession who signed the protest we have this choice bit from the *Louisville Medical Journal*, June, 1850. ". . . The prudish 'Miss Nancies' of Buffalo, have, unintentionally, conferred a benefit on the medical profession. Their excessive modesty and shamefacedness have aroused attention to the subject of clinical midwifery, and this attention will urge forward the good work. We can easily imagine an innocent childlike simplicity that would put pantalets upon the legs of a piano, and that would screen with a veil everything capable of exciting prurient ideas; but we do not like to see this excessive flirtation with modesty, introduced into medical teaching. A misplaced irritation of the blushing organs operated upon the seventeen Buffalo doctors and induced them to ease their tender consciences by a protest. May the Heavens smile serenely over their innocent slumbers. But while they sleep with Rip Van Winkle devotion, or with Barney O'Rierdon's 'attention,' we pray them not to disturb medical teaching with their snoring. They may sleep as much as they please, but the profession should be awake. The oil in the lamps of the 'seventeen' foolish virgins may burn out, but we wish to see the lights of the profession continually replenished, so that perpetual lamps may be lighting the path of progression." Space does not permit us to give more of this important and interesting controversy. In the end the opponents to clinical obstetrics burned themselves out and White continued his demonstrations to emerge a true pioneer in the teaching of clinical obstetrics.

Our attention to James P. White deserves further consideration, for he was not only a great force for the advancement of scientific medicine by his teaching and clinical work but to him belongs the real credit for first bringing to the attention of the medical profession the successful treatment of chronic uterine inversion. His work in this connection certainly appears to invalidate the generally accepted opinion that this priority belongs to Tyler Smith of London. White's first<sup>9</sup> case of successful reposition of the inverted uterus was reported before the Buffalo Medical Association on February 12, 1856, and appears in the published proceedings of that body. This was two years before Tyler Smith's<sup>10</sup> contribution. In 1858 the same year as Smith's publication White reported another successful reduction and later commented as follows,<sup>11</sup> "Tyler Smith in London on April 24, 1858, published in the *London Medical Times and Gazette* an account of a successful operation for inversion, but I submit that this was forty-two days after my operation in Hornellsville and more than two years after I had taken the initiative and had published my views and 'hopes' in connection with the report of a case of eight days' duration." White's original method consisted of manual pressure and counterpressure continued over a comparatively long period, i.e., hours. Later he added to his maneuver the use of a stem repositor. In 1876<sup>11</sup> he reported the twelve successful cases of uterine reposition one of which was of twenty-two years' duration and another of fifteen years' duration.

White's name is also associated with the obstetrical forceps,<sup>12</sup> having described a modified instrument in 1849. A plate showing this instrument may be found in Das' *Obstetrical Forceps, Its History and Evolution*,<sup>13</sup> The essential features

were the lightness of its construction, its very excellent cephalic curve, and the form of the fenestra.

The influence of the life and work of James P. White comes down to us to mark him as one of the leaders of obstetrics and gynecology of his generation. From Puritan stock, he was descended from Peregrine White,<sup>14</sup> the first child born in the Plymouth Colony. His grandfather was a soldier in the Revolution, and his father, David Pierson White, fought in the War of 1812. James Platt White was born in Austerlitz, Columbia County, New York, on March 14, 1811. His early education was in the schools and academies of western New York, and he spent some time under the tuition of Rev. John C. Lord. For a while the young man read law under his uncle, but this was soon abandoned in favor of medicine. White first attended medical lectures at the Fairfield Medical College in 1831 and later at the Jefferson Medical College where he was graduated in 1834. Previous to graduation, while yet a student, he was asked to practice at Black Rock, now a part of Buffalo, during a cholera epidemic in 1832. Following graduation he settled in Buffalo where in 1836 he married Mary Elizabeth Penfield of Penfield, New York. Shortly after this he met with a remarkable accident. While travelling in a stage coach over a very rough road, he was thrown against the top of the vehicle with such force as to fracture the atlas. Fortunately there was no displacement and after a long time, according to his biographer, Austin Flint,<sup>14</sup> the entire segment of the atlas was expectorated. He recovered, however, with the permanent loss of the power of rotation of the head upon the neck. The establishment of the University of Buffalo was largely due to White's exertions. Authority<sup>15</sup> states, "Frank H. Hamilton, Austin Flint, James P. White, Thomas N. Foote were among the physicians who first brought prestige to the city, and they with sympathetic laymen were the founders of the University of Buffalo. It was the physicians present at the first meeting who, after hot debate, persuaded the other members of the group to attempt not only a medical school, but a university with powers as complete and diversified as those possessed by any in the land." The same authority states, "for forty years the medical department comprised all there was of the university, it was known not as the Buffalo Medical College, but as the University of Buffalo." When the first faculty was organized, James P. White was chosen Professor of Obstetrics and Diseases of Women and Children. His association with this chair continued up to the time of his death. Although his early attempts to introduce clinical teaching in obstetrics involved a long and bitter professional struggle, he later became a recognized authority in his field, and in 1870 during the illness of Professor George T. Elliott he was invited to give a course of lectures on obstetrics at the Bellevue Hospital Medical College. This he did, not only declining to have his expenses borne by the college but giving the income from his lectures to his sick colleague. White was not only an eminently successful teacher of obstetrics, but he was recognized as a particularly competent surgeon, performing all the important operations in the gynecologic surgery of his day which included over a hundred ovariectomies.

As a writer in medicine, he published numerous articles in the medical journals of his day, the most noteworthy of which were those on chronic inversion of the uterus already referred to. Medical honors also came to this leader in medicine. He was chairman of the section on Obstetrics and Diseases of Women and Children of the American Medical Association in 1877, and in 1878 was elected first vice president of that organization. He was president of the New York State Medical Society in 1870 and was a Founder of the American Gynecological Society. White was also a leader in the civic activities of his community as witnessed by share in founding such bodies as the Young Men's Association, the Academy of Fine Arts, the Historical Society, the Buffalo Hospital of the Sisters of Charity, and the

Maternity and Foundling Hospitals. In reviewing his life and accomplishments we are impressed not only with his important contributions to our science but particularly with his great personal worth. James Platt White seems to have fulfilled in every way the definition set down by the Sage of Concord, "he is great who is what he is from nature, and who never reminds us of others." He died September 28, 1881.

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**Jacobsen: Fate of Endometrial Emboli in the Venous Circulation of the Rabbit,**  
Arch. Path. 15: 1, 1933.

To determine the fate of injected endometrial transplants, Jacobsen introduced autologous endometrial tissue into the venous circulation. Such material was obtained from 11 rabbits and included the "resting" stage of the cycle, in "heat," postpartum and pregnancy. Histologic studies of the tissues were made after thirty seconds (immediately) and varied further from twelve hours to one hundred and thirty days after operation.

The bulk of the cellular material was apparently filtered out in the pulmonary arterioles and capillaries, no adventitious cells being found in the heart, spleen, kidneys, or liver. Embolic cells could be recognized one week after injection but none could be identified after that. Stromal cells possibly survive longer than epithelium; fibrin is deposited about the cell emboli, their cytoplasm disappears, their nuclei become pyknotic and the embolus becomes converted into a hyaline mass in the smaller vessels and organized in the large arterioles. Complete absorption or autolysis results in clearing of the pulmonary vessels of the autologous cell masses with no suggestion of formation of new endometrial tissue. The results are in agreement with the distribution of characteristic lesions in cases of human ectopic endometriosis.

W. B. SERBIN.



# Department of Maternal Welfare

CONDUCTED BY FRED L. ADAIR, M.D., CHICAGO, ILL.

## A STATISTICAL STUDY OF 129,539 BIRTHS IN IOWA, WITH SPECIAL REFERENCE TO THE METHOD OF DELIVERY AND THE STILLBIRTH RATE\*

E. D. PLASS, M.D., IOWA CITY, IOWA, AND H. J. ALVIS, M.D.,  
ST. LOUIS, MO.

(From the Department of Obstetrics and Gynecology, State University of Iowa,  
College of Medicine)

**E**ARLY in 1930, through the cooperation of Dr. D. C. Steelsmith, Commissioner of Health for the state of Iowa, the standard birth certificate was amplified for use in the state by the addition of three questions: (a) "30—Character of delivery? Spontaneous? Operative? If operative, name type of operation performed"; (b) "31—Was child asphyxiated? Slightly? Moderately? Severely?"; and (c) "32—At what period of pregnancy did patient first consult you?" Replies to the last two questions proved of little value, but the first was completed for approximately three-fourths the births. This report deals with certain data obtained from a study of all birth certificates returned to the State Department of Health during the calendar years 1930, 1931, and 1932, and concerns especially the available information bearing upon the method of delivery and the stillbirth rate.

*Method of Analysis.*—Pertinent medical data from the birth certificates were placed on punch cards according to a numerical code and were analyzed by the usual procedure.

### GENERAL DATA

During the three years under consideration, 129,604 births were reported, but 65 certificates were so defective that they were discarded.

*Type of Pregnancy.*—The 129,539 useful certificates represented 128,238 pregnancies according to the following tabulation:

Single pregnancies	126,948	Ratio
Twin pregnancies	1,277	1: 100
Triplet pregnancies	13	1:10,000

The ratio of multiple pregnancies is slightly lower than that usually found but the difference is probably not significant.

*Sex of the Child.*—The sexes were represented as follows:

Males	66,801
Females	62,512
Sex not recorded	226

\*This investigation was made possible through funds obtained from the Division of Maternal and Infant Hygiene of the State University of Iowa.

The usual preponderance of male children is noted, with the ratio (106.86 males to 100 females) that which is commonly found in large compilations (106 or 107 to 100).

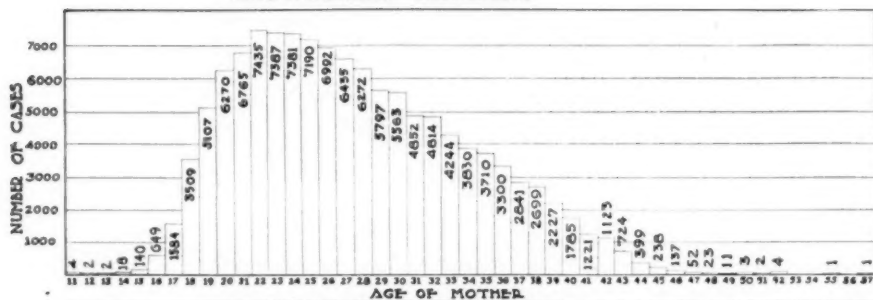
*Period of Uterine Gestation.*—Statements concerning the maturity of the child were available on 94,962 certificates. Among this group there were 5,012 premature infants, an incidence of 5.28 per cent.

*Stillbirths.*—There were 3,820 stillbirths among 129,519 reports, an incidence of 2.94 per cent. These stillbirths will be analyzed in a later section of this report.

*Legitimacy.*—Among 126,710 cases in which note was made of the legitimacy of the child, there were 2,599 illegitimates (2.05 per cent).

*Parity of the Mother.*—Because of an error in punching the cards for the second eighteen-month period, data on parity of the mother are available on only approxi-

### AGE DISTRIBUTION OF MOTHERS LEGITIMATELY PREGNANT



### ILLEGITIMATELY PREGNANT

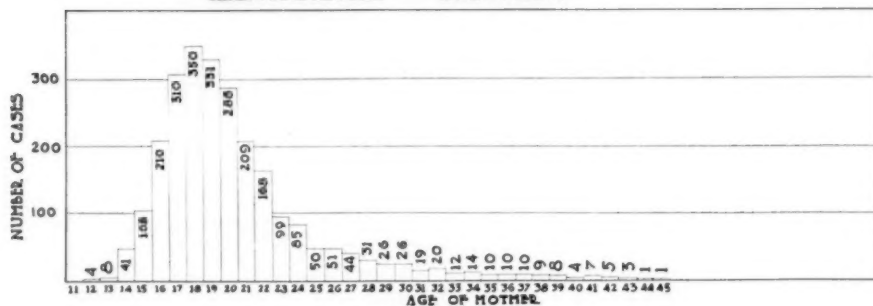


Chart 1.

mately one-half the births. Among 62,351 useful certificates, 14,861 recorded first children and 47,490 other than first children. This determined ratio of 1:3.2 probably represents the normal for the state under present conditions. No attempt was made to subdivide the multipara according to the number of children each had previously borne.

*Size of Community.*—Iowa is essentially a rural state and has only twenty-one cities with more than 10,000 population, according to the 1930 official census. These twenty-one communities included 716,523 individuals, while the remaining 1,754,416 inhabitants resided in small villages and towns or on farms. Births in the urban centers (more than 10,000 population) numbered 43,444, while in the rural communities (under 10,000 population) there were 86,095 births recorded. The average yearly birth rate for the three years in the state as a unit was 19.0 per 1,000 population; in the urban areas it was 20.2 per 1,000 as against 16.4 per 1,000

in the rural communities. The higher rate in the cities is probably attributable to the fact that many women from smaller communities and farms prefer to be delivered in the hospitals of nearby larger cities.

*Place of Birth.*—For the state as a whole, there were 41,418 hospital births out of a total of 129,539, a percentage of 32.0. In urban communities, 61.9 per cent of all births occurred in hospitals, while in the rural districts the percentage was only 16.9.

*Age of Mother.*—Among the 128,303 cases where the age of the mother was given, there was a spread from eleven to fifty-seven years. Certain of the higher ages reported are open to question and can probably be explained by the fact that many ignorant individuals have no accurate knowledge of their ages. The "mode" for all deliveries was twenty-two years, while among 2,572 illegitimate pregnancies the "mode" was eighteen years (Chart 1).

#### METHOD OF DELIVERY

Of the total of 129,539 births the type of delivery was specified in 91,738 cases (70.8 per cent) as being spontaneous, low forceps, midforceps, high forceps, breech extraction, version and extraction, cesarean section, craniotomy, or "operative—type not specified." Differentiation among the various varieties of forceps was obviously so defective that it was considered wise to group all forceps deliveries under the single heading.

*General Operative Incidence.*—Among the 91,738 deliveries in this series, 10,818 were operative in character, a gross operative incidence of 11.8 per cent. Analyses of these cases, made from various points of view, will be presented. It should be kept in mind that totals in the different studies may not agree because all the data were not uniformly available.

*Size of Community and Place of Delivery.*—The data are divided into hospital and home births in communities over and under 10,000 population in Table I.

TABLE I. NINETY-ONE THOUSAND SEVEN HUNDRED AND THIRTY-EIGHT DELIVERIES ACCORDING TO THE SIZE OF COMMUNITY AND HOME OR HOSPITAL

TYPE OF DELIVERY	STATE-WIDE	COMMUNITIES OVER 10,000			COMMUNITIES UNDER 10,000		
		TOTAL	HOSPITAL	HOME	TOTAL	HOSPITAL	HOME
Spontaneous	80,920 (88.2%)	25,115 (83.0%)	14,146 (76.9%)	10,969 (92.5%)	55,805 (90.8%)	10,273 (86.0%)	45,532 (91.9%)
Operative	10,818 (11.8%)	5,136 (17.0%)	4,247 (23.1%)	889 (7.5%)	5,682 (9.3%)	1,672 (14.0%)	4,010 (8.1%)
Totals	91,738	30,251	18,393	11,858	61,487	11,945	49,542
Delivered in hospital			60.8%			19.5%	

The higher operative incidence in the cities, especially in urban hospital practice, may be partially explained by a natural influx of complicated cases, but in all probability the greater burden must be borne by those practitioners who adhere to the doctrines of "prophylactic forceps," "elective versions," and other similar widely advertised forms of interference designed particularly to conserve the physician's time.

*Sex of the Child.*—Among 47,431 male children with the method of birth specified, 6,048 were operative in character, 12.8 per cent, whereas among 44,187 female children, 4,759, or 10.8 per cent, were born after assisted deliveries. The higher operative incidence among male children may probably be explained by the heavier weights and harder heads commonly attributed to this sex. We have no evidence in these data to support such a conclusion, but we must obviously seek an explanation in the children themselves rather than in their mothers.

*Period of Uterine Gestation.*—Of all specified deliveries 5.28 per cent were premature. Among these 5,012 premature births, the type of delivery was noted in 3,769 cases, with an operative rate of 16.8 per cent, as compared with 11.7 per cent in 72,837 full-term deliveries. Among 67,483 spontaneous births the prematurity rate was 4.6 per cent as against 6.9 per cent in 9,123 operative cases. The higher operative rate in premature births may be explained by the greater prevalence of serious complications of pregnancy during the seventh and eighth calendar months of gestation.

*Stillbirths.*—The general stillbirth rate was 2.94 per cent. Among 80,920 spontaneous births it was 2.0 per cent as compared with 8.0 per cent in 10,818 operative deliveries. The incidence of operative delivery among 89,270 live births was 11.2 per cent, while among 2,468 stillbirths it was 35.1 per cent. This association of a high stillbirth rate with operative delivery is surely significant and may be partly explained by the obvious fact that complications of pregnancy demanding delivery often of themselves prejudice the child's chances for life. On the other hand, the relatively high operative incidence for the entire group would indicate that many "convenience" operations were performed, and it is believed that they generally endanger the child's life to a certain extent. In urban hospitals where the operative incidence was 23.1 per cent, the total stillbirth rate was 3.9 per cent, as against a rural hospital rate of 14.0 per cent with 2.7 per cent stillbirths.

*Legitimacy.*—The illegitimacy rate for the entire series was 2.05 per cent. It is fair to assume that most of these deliveries occurred in hospitals although our data were not analyzed to elicit this information. Operative interference occurred in 13.4 per cent of illegitimate pregnancies as compared to an operative rate of 11.8 per cent in 88,466 legitimate deliveries. The difference may well be due to the higher proportion of primigravidas in the former group.

*Parity.*—For reasons stated earlier, it is possible to differentiate first labors from other-than-first labors in only a portion of the total series. In this group there were 9,836 primiparas with an operative incidence of 23.2 per cent, and 30,306 multiparas with an operative incidence of 6.5 per cent.

The operative incidence is twice as high among primigravidas and four times as high in multigravidas delivered in hospitals as among those cared for in the homes. When reasonable consideration is given to complications in hospitalized patients, it is still obvious that "convenience" procedures are a significant factor in hospital cases. The stillbirth rate varies with the operative incidence, emphasizing again that spontaneous birth is easiest for the child.

*Multiple Pregnancy.*—Among 89,886 single children with method of delivery specified, there were 10,522 cases of operative intervention, 11.7 per cent. In 1,825 reports covering the birth of children in twin pregnancies, 290 specified operative delivery, 15.9 per cent, while in 27 births covering 9 sets of triplets there were six operations, 22.2 per cent. The higher incidence of operative delivery in multiple pregnancies is readily explained by the common practice of extracting the second or third child after podalic version through thoroughly dilated passages rather than awaiting spontaneous expulsion.

#### ANALYSIS OF OPERATIVE DELIVERIES

Among the 91,738 cases with type of delivery specified, the operative incidence was 11.8 per cent. These 10,818 operations were distributed as shown in Table II.

The high percentage of forceps among all operative deliveries was anticipated since the general practitioner uses this method of terminating labor to the exclusion of other procedures. The relatively high number of versions, making it the second most common operative procedure, can be explained by the presence in the state of several obstetric specialists who advocate and practice elective version. The general

incidence of 1.0 per cent of cesarean section throughout the state indicates that this operation is being used too frequently, while the occurrence of 57 stillbirths (6.0 per cent) among the 955 cases of abdominal delivery emphasizes a widespread disregard for proper indications for the procedure. It is interesting that the author in a report to the White House Conference (1931) assumed from the incomplete evidence then available that the cesarean section incidence throughout the country

TABLE II. DISTRIBUTION OF 10,818 OPERATIVE DELIVERIES OCCURRING AMONG 91,738 CASES WITH TYPE OF DELIVERY SPECIFIED

TYPE OF OPERATIVE DELIVERY	NUMBER	PERCENTAGE OF ALL DELIVERIES	PERCENTAGE OF ALL OPERATIONS
Forceps—all varieties	6,474	7.1	59.8
Version and extraction	1,236	1.4	11.4
Cesarean section	955	1.0	8.8
Breech extraction	711	0.8	6.6
Craniotomy	4	0.004	0.04
Operative—not specified	1,438	1.6	13.3
Totals	10,818	11.904	99.94

was approximately 1.0 per cent. The relatively low incidence of breech extractions reported would indicate that, in general, breech deliveries are handled conservatively since in all probability these presentations occurred with the usual frequency (3 to 4 per cent). The performance of only four craniotomies in such a large series of cases leads to the belief that this operation is not employed frequently enough, and that patients who should have been delivered in this fashion are subjected to cesarean section, difficult forceps, or version. On the basis only of the probable incidence of hydrocephalus (1 to 2,000 or 3,000), one would expect more craniotomies. The "operative—type not specified" group is undoubtedly composed mostly of forceps deliveries, but in the absence of data to substantiate this view it was thought best to treat them separately.

*Size of Community and Place of Delivery.*—In communities of over 10,000, all operations except craniotomy and "operation—type not specified" were more frequently employed, with the operative furor confined entirely to hospitalized patients since the difference between the percentages of operative deliveries in homes in urban and rural communities is not significant. It should be noted that among all patients in urban communities the cesarean section incidence was 2.0 per cent, twice that for the state at large, and that among patients in hospitals the percentage rose to 3.2. There would seem to be little justification for such a high rate of abdominal delivery in a state where a contracted pelvis of any real significance is rarely met. The conclusion is again inevitable that a large number of unnecessary and ill-advised operations are being performed.

*Period of Uterine Gestation.*—Premature and full-term deliveries can be related to the method of delivery in 76,606 cases (Table III).

It is rather surprising to find that the operative incidence is higher in premature deliveries than in the full-term group and that the difference obtains for all types of operations except forceps and craniotomy. The fact that 3.5 per cent of all stated premature deliveries were effected by cesarean section is particularly disconcerting since it indicates a common practice of treating accidental complications of pregnancy by abdominal delivery. Obviously very few such operations can be justified by the classical indications for cesarean section—contracted pelvis or by the most usual indication in conservative clinics, a previous abdominal delivery—and the vast majority must have been performed because of "a desire to do something" in the presence of some complication. The stillbirth rate of 15.2 per cent for the group of



premature children born by cesarean section offers sufficient evidence that the operation is not especially effective as a child-life-saving procedure although its possibilities in this direction are commonly offered as justification for the operation.

TABLE III. THE PERIOD OF UTERINE GESTATION IN RELATION TO THE METHOD OF DELIVERY

TYPE OF DELIVERY	FULL TERM		PREMATURE	
	NUMBER	PER-CENTAGE	NUMBER	PER-CENTAGE
Spontaneous	64,348	88.4	3,135	83.2
Operative—total	8,489	11.6	634	16.8
Total	72,837	100.0	3,769	100.0
Forceps—all varieties	5,277	7.2	206	5.5
Version and extraction	954	1.3	124	3.3
Cesarean section	660	0.9	132	3.5
Breech extraction	535	0.7	85	2.2
Craniotomy	2	0.003	0	0.0
Operative—type not specified	1,061	1.4	87	2.3
Total	8,489	11.5	634	16.8

TABLE IV. PARITY OF MOTHER IN RELATION TO METHOD OF DELIVERY

TYPE OF DELIVERY	PRIMIPARAS		MULTIPARAS	
	NUMBER	PER-CENTAGE	NUMBER	PER-CENTAGE
Spontaneous	7,553	76.8	28,346	93.5
Operative—total	2,283	23.2	1,960	6.5
Total	9,836	100.0	30,306	100.0
Forceps—all varieties	1,556	15.8	989	3.3
Version and extraction	168	1.7	318	1.0
Cesarean section	151	1.5	199	0.7
Breech extraction	89	0.9	171	0.6
Craniotomy	0	0.0	0	0.0
Operative—type not specified	319	3.2	283	0.9
Totals	2,283	23.1	1,960	6.5

TABLE V. SIZE OF COMMUNITY AND PLACE OF DELIVERY IN RELATION TO PARITY OF MOTHER AND METHOD OF DELIVERY—PRIMIPARAS

TYPE OF DELIVERY	COMMUNITIES OVER 10,000				COMMUNITIES UNDER 10,000			
	HOSPITAL		HOME		HOSPITAL		HOME	
	NO.	PER-CENT-AGE	NO.	PER-CENT-AGE	NO.	PER-CENT-AGE	NO.	PER-CENT-AGE
Spontaneous	1,790	66.5	785	81.0	608	63.3	4,370	83.8
Operative—total	903	33.5	184	19.0	352	36.7	844	16.2
Total	2,693	100.0	969	100.0	960	100.0	5,214	100.0
Forceps, all varieties	584	21.7	129	13.3	245	25.5	598	11.5
Version and extraction	116	4.3	17	1.8	6	0.6	29	0.6
Cesarean section	95	3.2	4	0.4	40	4.2	12	0.2
Breech extraction	37	1.4	10	1.0	12	1.3	30	0.6
Craniotomy	0	0.0	0	0.0	0	0.0	0	0.0
Operative—type not specified	71	2.6	24	2.5	49	5.1	175	3.3
Totals	903	33.2	184	19.0	352	36.7	844	16.2

*Parity of the Mother.*—As previously stated it is possible to use only those patients (approximately one-half of the entire series) in whom the parity is accurately known.

When the method of delivery is considered in relation to the parity of the mother, the size of the community and the place of birth, the data in Tables V and VI are developed.

TABLE VI. SIZE OF COMMUNITY AND PLACE OF DELIVERY IN RELATION TO PARITY OF MOTHER AND METHOD OF DELIVERY—MULTIPARAS

TYPE OF DELIVERY	COMMUNITIES OVER 10,000				COMMUNITIES UNDER 10,000			
	HOSPITAL		HOME		HOSPITAL		HOME	
	NO.	PER-CENT-AGE	NO.	PER-CENT-AGE	NO.	PER-CENT-AGE	NO.	PER-CENT-AGE
Spontaneous	3,931	84.5	4,176	96.0	1,610	84.0	18,629	96.1
Operative—total	719	15.5	175	4.0	307	16.0	759	3.9
Total	4,650	100.0	4,351	100.0	1,917	100.0	19,488	100.0
Forceps—all varieties	331	7.1	72	1.7	183	9.5	403	2.1
Version and extraction	168	3.6	44	1.0	22	1.2	84	0.4
Cesarean section	108	2.3	5	0.1	64	3.3	22	0.1
Breech extraction	45	1.0	24	0.5	16	0.8	86	0.4
Craniotomy	0	0.0	0	0.0	0	0.0	0	0.0
Operative—type not specified	67	1.5	30	0.7	22	1.2	164	0.9
Totals	719	15.5	175	4.0	307	16.0	759	3.9

Among primiparas there is a relatively high incidence of operative delivery in all groups and especially when confinement occurs in a hospital. Forceps deliveries account for approximately two-thirds of the operations. Version and extraction is more often employed in urban practice than in the rural districts. The high cesarean section rate in hospital practice is worthy of note, as is the fact that abdominal deliveries are still being performed in homes, even in a state where hospitals are easily available.

Among multiparas the operative incidence is relatively low, but in hospital practice one multipara in every six is delivered artificially. The high incidence of cesarean section (2.3 and 3.3 per cent) among hospital cases should also be noted. For all multiparas, irrespective of the place of delivery, this rate is 0.7 per cent as against 1.5 per cent for the primiparas.

TABLE VII. SEX OF THE CHILD IN RELATION TO METHOD OF DELIVERY

TYPE OF DELIVERY	MALES		FEMALES	
	NUMBER	PERCENTAGE	NUMBER	PERCENTAGE
Spontaneous	41,383	87.2	39,428	89.2
Operative—total	6,048	12.8	4,759	10.8
Total	47,431	100.0	44,187	100.0
Forceps—all varieties	3,705	7.8	2,764	6.3
Version and extraction	665	1.4	569	1.3
Cesarean section	510	1.1	444	1.0
Breech extraction	363	0.8	347	0.8
Craniotomy	2	0.004	2	0.004
Operative—not specified	803	1.7	633	1.4
Totals	6,048	12.8	4,759	10.8

*Sex of the Child.*—It has already been observed that operative delivery is more common when the child is a male (12.8 per cent) than when it is of the opposite sex (10.8 per cent). With the ratio of the sexes in the entire series 106.86 males to

100.0 females; the ratio in spontaneous delivery is 104.96 to 100.0, and in operative deliveries 127.09 to 100.0.

The increased percentage of operative birth among male children over females obtains for all operative procedures except breech extraction and craniotomy in which cases the sex presumably is not a factor in the production of the presentation nor in the development of the anomaly necessitating these two procedures.

*Multiple Pregnancy.*—It has been previously noted that, as might have been expected, the operative incidence is higher in the presence of multiple pregnancy.

TABLE VIII. MULTIPLE PREGNANCY IN RELATION TO METHOD OF DELIVERY

TYPE OF DELIVERY	TWINS		TRIPLETS	
	NUMBER	PERCENTAGE	NUMBER	PERCENTAGE
Spontaneous	1,535	84.1	21	77.8
Operative—total	290	15.9	6	22.2
Total	1,825	100.0	27	100.0
Forceps—all varieties	102	5.6	2	7.4
Version and extraction	70	3.8	2	7.4
Cesarean section	22	1.2	0	0.0
Breech extraction	67	3.7	1	3.7
Craniotomy	0	0.0	0	0.0
Operative—not specified	29	1.6	1	3.7
Total	290	15.9	6	22.2

The incidence of cesarean section in multiple pregnancy (1.2 per cent) is relatively low when it is considered that this procedure was carried out on only 11 mothers with twin pregnancies and in none with triplets. The high incidence of version, 3.8 per cent, can be explained by assuming that delivery of the second twin was frequently completed in this fashion, while the high percentage of breech extractions points to an increased incidence of breech presentations in multiple pregnancies, a fact which is generally recognized.

*Legitimacy.*—Among the 2,599 illegitimate births the parity of the mothers is not available, but it is probably safe to assume that the proportion of primiparity is higher than in the legitimate group. The method of delivery in the legitimately and the illegitimately pregnant is shown in Table IX.

TABLE IX. LEGITIMACY IN RELATION TO METHOD OF DELIVERY

TYPE OF DELIVERY	LEGITIMATE		ILLEGITIMATE	
	NUMBER	PERCENTAGE	NUMBER	PERCENTAGE
Spontaneous	78,041	88.2	1,685	86.6
Operative—total	10,425	11.8	260	13.4
Total	88,466	100.0	1,945	100.0
Forceps—all varieties	6,231	7.0	171	8.8
Version and extraction	1,208	1.4	14	0.7
Cesarean section	928	1.0	16	0.8
Breech extraction	675	0.8	23	1.2
Craniotomy	4	0.005	0	0.0
Operative—not specified	1,379	1.6	36	1.9
Totals	10,425	11.8	260	13.4

There is a significant increase in the number of forceps and of breech extractions among the illegitimates; this may well be related to the higher proportion of primiparas. On the other hand, the lower incidence of version and extraction and of cesarean section may indicate a tendency toward less interference among this group, presumably cared for in large part as charity patients.

*Stillbirths.*—Stillbirth data are available even though there are no figures for neonatal deaths; their relation to the type of delivery is shown in Table X.

TABLE X. STILLBIRTHS IN RELATION TO METHOD OF DELIVERY

TYPE OF DELIVERY	TOTAL BIRTHS WITH AVAILABLE DATA	STILLBIRTHS	
		NUMBER	PERCENTAGE
Spontaneous	80,920	1,602	2.0
Operative—total	10,818	866	8.0
Total	91,738	2,468	2.7
Forceps—all varieties	6,474	328	5.1
Version and extraction	1,236	243	19.6
Cesarean section	955	57	6.0
Breech extraction	711	78	11.0
Craniotomy	4	4	100.0
Operative—type not specified	1,438	156	10.8
Totals	10,818	866	8.0

The stillbirth rate in operative deliveries is four times as high as in spontaneous births. Delivery by the feet (version and extraction, and breech extraction) carries an almost prohibitive risk for the child, the former resulting in the birth of dead children once in five times and with undoubtedly a considerable neonatal mortality from intracranial injury. If it were possible to exclude the "elective versions" performed by Potter's disciples, who admittedly have a more reasonable fetal mortality, the risk to the child must be close to 50 per cent. The complications for which this procedure is commonly recommended carry a serious risk to the child, but whether it is sufficiently great to elevate the fetal death rate to such a high point is debatable. It would rather seem that the general practitioner should be discouraged from employing internal podalic version.

A stillbirth rate of 6.0 per cent in cesarean section indicates that the operation is frequently performed on unsuitable cases, in which the child has already perished, and in which it is probable that delivery from below would at least carry a smaller risk to the mother. Unfortunately, the maternal death rate in this series of abdominal deliveries is not available; a plan is under consideration to determine it during the coming year by an intensive investigation of all known cases in this three-year period.

## ANALYSIS OF STILLBIRTHS

Among the entire group of 129,539 cases, there were 3,820 stillbirths, an incidence of 2.94 per cent. In the 37,801 births in which the type of delivery was not stated, the stillbirths numbered 1,352, a rate of 3.6 per cent, while among the 91,738 with delivery data available for analysis, there were 2,468 stillbirths, an incidence of 2.7 per cent. No explanation for the higher rate in the former group can be offered, except that physicians who fill out certificates carelessly are apt not to be careful professionally, a fact which would conduce to a higher stillbirth rate.

*Type of Delivery.*—Table X shows that the stillbirth rate is four times as high in operative as in spontaneous delivery, and that, especially in version and extraction and in breech extraction, the risk to the child is almost prohibitive.

*Size of Community and Place of Delivery.*—Data are available on the relation of stillbirths to the place of birth and the method of delivery. (Tables XII-A and XII-B.)

TABLE XI

SIZE OF COMMUNITIES	STILLBIRTH PERCENTAGES	
	HOSPITAL	HOME
Communities over 10,000	3.9	2.7
Communities under 10,000	2.7	2.7

For all the data, some of which could not be used in tabular form, the stillbirth rates prevailed as shown in Table XI.

The significant increase in the stillbirth rate in urban hospitals over that of the other groups is probably related to the increased incidence of operative delivery. The fact that the rate is lower in the rural hospitals, although presumably they treat a larger proportion of emergency cases, strengthens this opinion.

TABLE XII-A AND B. STILLBIRTHS IN RELATION TO SIZE OF COMMUNITY, PLACE OF BIRTH, AND METHOD OF DELIVERY

*Communities With Over 10,000 Population*

TYPE OF DELIVERY	HOSPITAL			HOME		
	TOTAL BIRTHS	STILLBIRTHS		TOTAL BIRTHS	STILLBIRTHS	
		NO.	%		NO.	%
Spontaneous	14,146	359	2.5	10,969	221	2.0
Operative—total	4,247	285	6.7	889	67	7.5
Total	18,393	644	3.5	11,858	288	2.4
Forceps—all varieties	2,381	101	4.2	529	28	5.3
Version and extraction	687	86	12.5	115	16	13.9
Cesarean section	584	25	4.3	33	4	12.1
Breech extraction	244	24	9.8	76	7	9.2
Craniotomy	2	2	100.0	0	0	0.0
Operative—type not specified	349	47	13.5	136	12	8.8
Totals	4,247	285	6.7	889	67	7.5

*Communities With Under 10,000 Population*

Spontaneous	10,273	123	1.2	45,532	899	2.0
Operative—total	1,672	128	7.7	4,010	386	9.4
Total	11,945	251	2.1	49,542	1,285	2.6
Forceps—all varieties	1,072	45	4.2	2,492	154	6.2
Version and extraction	97	35	36.1	337	106	31.5
Cesarean section	260	17	6.1	78	11	14.2
Breech extraction	74	6	8.1	317	41	12.9
Craniotomy	1	1	100.0	1	1	100.0
Operative—type not specified	168	24	14.3	785	73	9.3
Totals	1,672	128	7.7	4,010	386	9.4

Among the cases available for this more detailed study the various stillbirth rates arrange themselves in descending order as follows: (1) urban hospitals, (2) rural homes, (3) urban homes, and (4) rural hospitals. The urban stillbirth rates are higher for both hospitals and homes than those for the rural districts, where operative delivery is less commonly employed. It is noteworthy that the rate in urban hospitals is almost twice as high as that prevailing in rural hospitals in spite of the fact that the great majority of recognized specialists practice in the larger cities. Without any notable exceptions, the percentage of stillbirths incident to any one type of operative procedure is lower in both the hospitals and homes of the larger communities, and the rate for all operative deliveries is lower; but the increased incidence of operation affects the total stillbirth rate adversely. This would seem to indicate that urban physicians possibly have better operative technic but that they do not use as good judgment in deciding to terminate labor artificially. Such figures emphasize again the relationship between an increased operative incidence and a rising stillbirth rate.

*Period of Uterine Gestation.*—Among the 76,606 cases where statements were available concerning the maturity of the child and the type of delivery, the total stillbirth rate was 2.7 per cent.



TABLE XIII. STILLBIRTHS IN RELATION TO PERIOD OF UTERINE GESTATION AND METHOD OF DELIVERY

TYPE OF DELIVERY	FULL TERM			PREMATURE		
	TOTAL BIRTHS	STILLBIRTHS		TOTAL BIRTHS	STILLBIRTHS	
		NO.	%		NO.	%
Spontaneous	64,348	667	1.0	3,135	680	21.7
Operative—total	8,489	553	6.5	634	168	26.5
Total	72,837	1,220	1.7	3,769	848	22.5
Forceps—all varieties	5,277	237	4.5	206	41	19.9
Version and extraction	954	151	15.8	124	53	42.7
Cesarean section	660	30	4.5	132	20	15.2
Breech extraction	535	42	7.8	85	22	25.9
Craniotomy	2	2	100.0	0	0	0.0
Operative—type not specified	1,061	91	8.6	87	32	36.8
Total	8,489	1,220	6.5	634	168	26.5

Prematurity definitely prejudices the child's chances of survival, the stillbirth rate being thirteen times as great as among full-term children. Operative delivery is not as important a factor in premature stillbirths as is the case with mature children. Operation results in six and one-half times as many stillbirths among full-term children as does spontaneous birth, while among prematures the increased risk amounts to only approximately 25 per cent. Version and extraction, and breech extraction, with delivery of the after-coming head, stand out in both groups as being especially dangerous to child life.

An analysis of the data bearing upon the stillbirth rates of premature and full-term children in hospital and home practice is given in Table XIV.

TABLE XIV

MATURITY OF CHILD	PERCENTAGE OF STILLBIRTHS	
	HOSPITAL	HOME
Full term	1.9	1.7
Premature	24.7	24.4

The large part which prematurity plays in the causation of stillbirths is shown by the fact that among 94,962 cases there were 5,012 premature births, an incidence of 5.3 per cent. Among these 5,012 premature births, there were 1,231 stillbirths, which comprised 43.9 per cent of all stillbirths.

*Parity of the Mother.*—An analysis of the relation of parity to the stillbirth rate is presented in Table XV.

TABLE XV. STILLBIRTHS IN RELATION TO PARITY OF THE MOTHER AND TYPE OF DELIVERY

TYPE OF DELIVERY	PRIMIPARA			MULTIPARA		
	TOTAL BIRTHS	STILLBIRTHS		TOTAL BIRTHS	STILLBIRTHS	
		NO.	%		NO.	%
Spontaneous	6,269	131	2.1	48,378	900	1.9
Operative—total	2,006	120	6.0	3,629	357	9.8
Total	8,275	251	3.0	51,646	1,257	2.4
Forceps—all varieties	1,338	46	3.4	1,786	104	5.8
Version and extraction	174	24	13.8	651	130	20.0
Cesarean section	127	8	6.3	388	27	7.0
Breech extraction	92	15	16.3	353	29	8.2
Craniotomy	2	2	100.0	0	0	0.0
Operative, type not specified	273	25	9.2	451	67	14.9
Total	2,006	120	6.0	3,629	357	9.8

TABLE XVI. STILLBIRTHS IN RELATION TO PARITY OF THE MOTHER, PERIOD OF UTERINE GESTATION AND METHOD OF DELIVERY

TYPE OF DELIVERY	PRIMIPARA						MULTIPARA					
	FULL TERM			PREMATURE			FULL TERM			PREMATURE		
	TOTAL	STILLBIRTHS		TOTAL	STILLBIRTHS		TOTAL	STILLBIRTHS		TOTAL	STILLBIRTHS	
		NO.	%		NO.	%		NO.	%		NO.	%
Spontaneous	5,926	63	1.1	343	68	19.8	46,374	466	1.0	2,004	434	21.8
Total—operative	1,920	96	5.0	86	24	27.8	3,268	261	8.0	361	96	26.6
Total	7,846	159	2.0	429	92	21.4	49,632	727	1.5	2,365	530	22.4
Forceps—all varieties	1,301	42	3.2	37	4	10.8	1,698	86	5.1	88	18	20.5
Version and extraction	84	10	11.9	8	5	62.5	296	19	6.4	57	10	17.5
Cesarean section	167	20	11.4	7	4	57.1	554	90	16.3	97	40	41.2
Breech extraction	111	5	4.5	16	3	18.8	312	15	4.8	76	12	15.8
Craniotomy	2	2	100.0									
Operative—type not specified	255	17	6.7	18	8	44.4	408	51	12.5	43	16	37.2
Totals	1,920	96	5.0	86	24	27.8	3,268	261	8.0	361	96	22.4

The total stillbirth rate is 20 per cent less for multiparas than for primiparas, but when delivery is completed artificially, children of multiparous mothers have a considerably increased risk of being born dead. In all probability this condition is due to the fact that while operative delivery is much less common among multiparas the complications justifying and indicating intervention are of a more serious nature and impose a greater risk on the child. In each type of operation, except breech extraction, the stillbirth rate is higher among multiparas.

When parity of the mother and the period of uterine gestation are studied together in relation to the type of delivery, Table XVI is evolved.

With full-term children, primiparas show a higher stillbirth rate than multiparas, a difference which appears to some extent even when labor is completed spontaneously. Premature children of both groups of mothers have comparable stillbirth rates.

#### DISCUSSION

This study, which was begun with the belief that it would add something to our knowledge of the state of obstetric practice in a large governmental unit, has revealed certain facts of considerable significance.

1. The gross incidence of operative delivery was 11.8 per cent, while in the urban sections (communities of more than 10,000 population) it was 17.0 per cent as against 9.3 per cent in smaller communities.

2. Cesarean section was employed in 1.0 per cent of all deliveries, in 0.9 per cent of all full-term deliveries, and in 3.5 per cent of all premature births. In urban hospitals abdominal deliveries accounted for 3.2 per cent, and in rural hospitals for 4.2 per cent of all deliveries. Cesarean section was used to deliver 1.5 per cent of the primiparas and 0.7 per cent of the multiparas. Among 955 cesarean sections there were 57 stillborn children, an incidence of 6.0 per cent.

3. The ratio of primiparas to multiparas was 1 to 3.2. The operative incidence among primiparas (23.1 per cent) was almost four times as great as in multiparas (6.5 per cent). The stillbirth rate among primiparas was appreciably higher (3.0 per cent) than among multiparas (2.4 per cent).

4. Premature children represented 5.28 per cent of the total. The operative delivery incidence was 16.8 per cent as against 11.7 per cent among the full-term children, and the stillbirth rate 22.5 per cent as compared with 1.7 for the full-term group.

5. Prematurity and operative interference predispose to stillbirth. Premature children accounted for 43.9 per cent of all stillbirths. The stillbirth rate among full-term children increases in proportion to the operative incidence, so that it is highest in the urban hospitals where operative intervention is more commonly practiced.

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**Misgeld: Neuritis Following "Apiol" Medication.** *Deutsche med. Wchnschr.* 58: 1925, 1932.

Apiol is a proprietary abortive containing triortho-cresyle-phosphate. This ingredient is quite neurotoxic and now is held responsible for the polyneuritic complications not infrequently observed following the administration of the drug. A case is reported in which a bilateral paresis of the peroneal nerves and the muscles of the hand developed about two months after the self-administration of four capsules daily for seven days. The nervous disturbances were purely motoric.

G. E. GRUENFELD.

## Society Transactions

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### OBSTETRICAL SOCIETY OF PHILADELPHIA

*MEETING OF DECEMBER 7, 1933*

The following papers were presented:

**Fatal Eclampsia at the Fifth Month with Complete Autopsy.** Dr. Roland D. Porter. (For original article see page 257.)

**Banti's Disease Complicating the Puerperium.** Dr. Dorothy L. Ashton. (For original article see page 280.)

**Infrequent Complications of Uterine Cancer, with Certain Clinical Observations.** Dr. L. C. Scheffey. (For original article see page 214.)

**Transverse Position of Vertex Presentation.** Dr. R. B. Wilson.

**Endometriosis in Laparotomy Scars.** Dr. E. A. Schumann and Dr. W. E. Parke. (For original article see page 222.)

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### CHICAGO GYNECOLOGICAL SOCIETY

*MEETING OF DECEMBER 15, 1933*

The following case reports and papers were presented:

**Tuberculous Salpingitis Discovered Incidental to Salpingostomy.** Dr. A. B. Hunt. (See page 277.)

**Tuberculosis of the Fallopian Tubes, Uterus and Uterine Cervix.** Dr. C. D. Hauch. (See page 276.)

**Tuberculosis and Adenomyoma.** Dr. A. F. Lash. (See page 272.)

**Pregnancy in Tuberculosis.** Dr. G. T. Palmer. (By invitation.) (See page 173.)

**Oxygen-Pneumoperitoneum in the Diagnosis and Treatment of Tuberculous Salpingitis.** Dr. I. F. Stein.

**Secondary Lymphogranulomatosis Vulvae.** Dr. A. F. Lash. (See page 274.)

# Department of Reviews and Abstracts

CONDUCTED BY HUGO EHRENFEST, M.D., ASSOCIATE EDITOR

## Collective Review

### TRENDS IN GYNECOLOGY AND OBSTETRICS DURING 1933

J. P. GREENHILL, M.D., CHICAGO, ILL.

FOR the present review, I have selected only the more important subjects discussed before foreign and American gynecological and obstetrical societies.

#### ANALGESIA AND ANESTHESIA

In the opinion of Bemis (N.Y.O.S.),\* the usefulness of avertin in labor is limited by its frequent failure satisfactorily to relieve the patient of pain and at the same time allow labor to progress. The action of this drug is short and often the patients become extremely restless. However, it may safely and advantageously be used as a basal anesthetic in selected surgical cases because it produces complete amnesia and absence of immediate preoperative emotional agitation, it permits complete anesthesia with a lessened amount of ether, and it insures a comfortable postoperative convalescence. Cochran feels that avertin produces a successful state of analgesia or amnesia but in many cases more nursing is required than with the use of some of the other analgesics. Conaway does not consider this drug valuable in obstetrics but finds it useful in gynecology and general surgery. Holden has used avertin extensively in the last three years and warns that the patient must have the exclusive services of a nurse until she is entirely out of the anesthetic.

Brammer (U.R.O.G.S.) is in favor of combining pernocton (called Pernoston by the A.M.A. Council), twilight sleep, and oxytocics during labor because he obtained amnesia in 90 per cent of his cases. Castallo (O) also praises pernocton and minimizes the restlessness which occurs in some women. Colloridi (O) is convinced that basal narcosis produced by pernocton as a preliminary to general anesthesia has many advantages in operative gynecology, but he warns that it is not foolproof. Kelly (O) found that nembutal given in combination with chloral is of undoubted value in labor. Ekerfors (O) tried to duplicate the good effects claimed for dilaudid-scopolamine analgesia but found that in 40 per cent, the patients did not experience alleviation of their pains, and in a similar proportion of cases, the uterine contractions diminished in intensity. Van Del (O) observed that sodium amytal is a satisfactory analgesic in labor but cannot be depended upon in all cases. Furthermore, because of restlessness, careful nursing supervision is necessary. Moore (W.D.M.S.) believes the best results in labor are obtained not by one analgesic but by a combination of drugs.

Evipan, a drug which is administered intravenously, has been used extensively in Germany during the past year. Ansehütz (G.S.S.) pointed out that it produces

\*For code see end of article.



rapid narcosis and permits quick awakening. Doerfler (B.O.G.S.) recommended evipan for short narcosis as did also Schulz (M.G.O.G.S.), Vogt (M.G.O.G.S. and S.G.O.G.S.), Metz (S.G.O.G.S.), Gocke (O) and Köster (O). On the other hand, while Küstner (M.G.O.G.S.) praised evipan for minor gynecologic operations he deprecated its use in labor because its action does not last long enough.

Roques (O) believes that the most suitable drug for the first stage of labor, having due regard to safety, ease of administration, and expense, is morphine. He favors chloroform during the second stage except in hospitals and for affluent women for whom he recommends gas oxygen and ether. Rivett (B.M.A.) also considers gas and oxygen as the ideal anesthetic when administered by an expert, but for the majority of women, he advocates chloroform to be used as an analgesic rather than as an anesthetic.

Margraf (M.R.O.G.S.) reported a series of 1,300 obstetric and gynecologic operations performed under nitrous oxide anesthesia. Ether had to be added in 80 per cent of the cases where the procedures were extensive, and the author attributes three deaths to the anesthetic. Strassmann found nitrous oxide satisfactory for gynecologic operations but in obstetrics he preferred chloroform and spinal anesthesia.

Haupt and Kraus (M.R.O.G.S.) favor sacral anesthesia in cases where inhalation and rectal anesthesia are contraindicated in spite of the fact that this form of anesthesia was successful in only 52 per cent of their abdominal operations.

According to Sabate (A.G.O.F.L.), spinal anesthesia with percaine is the ideal anesthesia for obstetric and gynecologic cases. However, it should not be employed in cases where version is to be performed or in women with eclampsia. Sabel (O.S.P.) found spinal anesthesia as safe as inhalation anesthesia in selected cases but Mann quoted the figures from his hospital which indicate that whereas there were three deaths among 7,000 ether and nitrous oxide anesthetics there occurred three fatalities among 727 spinal anesthetics. Akei (K.G.S.) is of the opinion that there are few contraindications to spinal anesthesia but Yagi and Oga (K.G.S.) reported two deaths in a series of 50 gynecologic operations. Preissecker (S.G.O.G.S.), after having observed six deaths in a series of 1,500 spinal anesthetics, came to the conclusion that this form of anesthesia should not be used where inhalation is contraindicated because the contraindications are the same for both. In fact, the indications and contraindications for spinal anesthesia should be more carefully observed because the risks are greater. Wladika (N.G.G.S.) believes that Pitkin's method of controllable spinal anesthesia is a distinct advance in this form of anesthesia.

Heard (C.M.A.) obtained good results with spinal anesthesia in cesarean sections, but because of its dangers, Sabel (O.S.P.) abandoned this form of anesthesia for these operations. Benthin (N.G.G.S.) considers spinal anesthesia too dangerous for pregnant women. Mavromati (B.G.S.) maintains that accidents occur with spinal anesthesia because after its use there may result paralysis of the sympathetic system, a meningeal reaction, a toxic effect on the nerve cells and shock.

Franken (G.G.S.) proved that spinal anesthesia is dangerous for a woman in labor by demonstrating that during each pain when the patient makes expulsive efforts, the pressure in the spinal column increases and brings the anesthetic near to the danger zone of the medulla oblongata. Coughing, pressing downward and unrest may do the same thing. Furthermore, during gestation there is an increased blood reservoir in the splanchnic vessels and since spinal anesthesia produces a paralysis of the lower half of the body and especially of the region of the splanchnic

vessels, it is easy to see how in pregnant women there may result a dangerous accumulation of blood in the splanchnic area with serious interference in the circulation of blood.

Frigysi (V.O.G.S.) described his method of local infiltration anesthesia for gynecologic operations and cesarean sections. This author uses narcosis only to supplement local anesthesia. Finsterer mentioned that he has used parasacral anesthesia in combination with injection of novocaine above the fifth lumbar vertebra in 4,500 cases. He never encountered a fatal case of intestinal paralysis, whereas he observed five deaths from this cause in 610 operations performed under general anesthesia. Latzko and also Adler perform all their vaginal operations under infiltration anesthesia, even those for carcinoma of the uterus. Keller mentioned that even in veterinary obstetrics, infiltration anesthesia is being used extensively, especially for cesarean sections and hysterectomies in small animals. Neuweiler (O) described in detail his technic for the use of infiltration anesthesia in the repair of perineal lacerations. Greenhill (S.M.A.) pointed out the advantages of direct infiltration anesthesia over inhalation and spinal anesthesia and showed why the former is the safest of all anesthetics. He described in detail the technic of infiltration anesthesia for all obstetric operations.

#### ENDOCRINOLOGY

At the annual meeting of the British Medical Association, Novak of Baltimore discussed the gynecologic aspects of endocrinology. He pointed out that the ovary produces two hormones. Folliculin (also called estrin, theelin and menformon) is the hormone of the graafian follicle. With the rupture of the follicle, the luteal phase of the cycle begins, the corpus luteum producing two hormones, folliculin and progesterin. Folliculin is, therefore, produced throughout the ovarian cycle, progesterin only after ovulation. Folliculin causes hyperemia and growth of the endometrium and progesterin is responsible for the secretory activity of the uterine glands. Typical periodic bleeding, menstrual in the clinical sense, may occur without ovulation, but this is not accompanied by the endometrial changes of genuine menstruation. It seems that the withdrawal of folliculin is the cause of menstrual bleeding. The structure governing pelvic changes is the anterior lobe of the pituitary. Novak emphasized that the results of gynecologic organotherapy have been disappointing. Prolan effectively controlled abnormal bleeding at puberty and the menopause and primary dysmenorrhea, while folliculin helped overcome the vasomotor symptoms at the menopause. Johnstone (B.M.A.) discussing the same subject pointed out that the Aschheim-Zondek test as performed at the University of Edinburgh yielded an accuracy of 99.1 per cent. Negative errors arose in cases which subsequently aborted and Johnstone has successfully treated cases of habitual abortion with luteinizing doses of hormone obtained from urine of pregnant women. He emphasized that the hormone of any endocrine gland was incapable of stimulating its parent gland so that hormone therapy was essentially substitutive; but the hormone of one gland might stimulate that of another gland.

Evans (C.A.P.S.) analyzed our knowledge of anterior pituitary function and referred to the fact that no portion of the hypophysis is essential for the continuance of life itself. He discussed the following hypophyseal hormones: growth, gonadotropic and lactogenic, thyrotropic, diabetogenic and adrenaltropic. In spite of the clarity of the presentation, the array of facts concerning the hypophyseal hormones is bewildering. Aschheim (R.S.M.) reviewed the subject of the female sex hormones and gonadotropic substances.

Falkiner (R.A.M.I.) reported on the structure and vascular conditions of the human corpus luteum in the menstrual cycle and in pregnancy, and showed that

hemorrhage occurs in the ovary twice during the menstrual cycle, in the follicle at the time of rupture and in the corpus luteum at or about the time of the onset of the menstrual flow. When hemorrhage occurs in the corpus luteum, it marks the end of its career as a gland of internal secretion. When pregnancy supervenes, no hemorrhage takes place and the corpus luteum persists as an active structure.

As Fluhmann (A.C.P.) pointed out, the term "ovary-stimulating hormone" is used for certain biologic substances which stimulate the growth of graafian follicles, ovulation and corpus luteum formation resulting in the production of the ovarian hormones, estrin and progesterin. The ovary-stimulating principles are chiefly in the anterior hypophysis but during pregnancy they are widely disseminated in the bodies of mother and fetus. They have also been demonstrated in the blood and urine of patients with amenorrhea, following castration, and in the postclimacteric period. From a clinical standpoint, three important advances have resulted from these studies: (1) the development of a test for the diagnosis of pregnancy and the control and treatment of hydatidiform mole and chorionepithelioma; (2) a new method of study of certain endocrinologic conditions which are accompanied by ovarian disturbances; and (3) the use of extracts of ovary-stimulating hormones for the successful treatment of the uterine hemorrhages accompanying hyperplasia of the endometrium.

Saethre (O) found prolactin in the urine of all but two of 114 old women but failed to find it in the urine of 25 young girls who had not yet begun to menstruate. Kosakae, Ohga and Okamoto (K.G.S.) found no difference in the amount of follicle hormone excreted in women with normal genitalia and those with hypoplasia of the uterus. The same authors (K.G.S.) found follicle hormone in each of ten women who had carcinoma, even in those past the menopause.

Fluhmann (S.F.B.C.O.G.S.) presented a study which suggests that the ovary-stimulating hormone found in the blood of pregnant women is not identical with that occurring in the anterior hypophysis of sheep. Collip, Selye, Anderson, and Thomson (A.M.A.) believe that the anterior pituitary-like hormone of pregnancy urine is derived from the placenta and is not necessarily identical with any truly hypophyseal principle. Experiments performed by Klingler, Burch and Cunningham (O) demonstrated that the ovary-stimulating properties of the anterior hypophysis can be increased by a placental extract which probably contains all three of Collip's fractions, while estrin, one of the components of the crude extract, definitely depresses the hypophysis. Aschheim and Hohlweg (B.S.G.) reported on the finding of estrogenic substances in bitumens.

Zondek (O) studied the action of folliculin and prolactin on the bat during hibernation and found that by means of these substances he could produce in this animal during winter all the phases of the generative process: estral reaction of the vaginal mucous membrane, conversion of the enlarged follicle into a corpus luteum, hyperluteinization and pregnancy.

Geist (A.G.S.) administered antuitrin-S to 50 women and in 33 instances observed changes in the ovaries characterized by marked congestion of the blood vessels and hemorrhagic extravasation.

In the monkey, Hartman (A.G.S.) found that over 100 precisely determined cases of ovulation occurred almost together on from the tenth to the fifteenth day of the cycle. An analysis of 53 cases, in which ovulation was recorded in complete cycles, shows that the preovulatory interval is relatively constant and that the variations in total cycle length parallel and are due almost altogether to variations in the length of the postovulatory interval. Hence, Ogino's suggestion that we count backward from the succeeding menstrual period to determine the ovulation day, need not worry us.

In 22 cases, Cotte and Colson (L.S.S.) transplanted ovaries into women in whom the uterus was conserved, and in every case but one, menopause was averted.

Kita and Okuni (K.G.S.) accelerated the secretion of milk in rabbits by first injecting urine of pregnant women and following this by pituitary extract. Litt (C.G.S.) transplanted pieces of placental tissue into the eye of rabbits and found no effect on the formation or secretion of milk.

Clauberg (N.E.G.G.S.) demonstrated the histologic changes in the endometrium of seven women to prove the effectiveness of corpus luteum hormones in human beings. Loeser (B.S.O.G.) produced menstruation in two women, one twenty-eight and the other thirty-eight years old, who had primary amenorrhea, by giving them 300,000 mouse units of folliculin followed by 50 rabbit units of corpus luteum. R. Meyer verified the histologic changes in the endometrium in these cases. Kaufman (B.S.O.G.) produced menstruation in a castrated woman by injecting 300,000 mouse units of ovarian hormone and 90 rabbit units of corpus luteum hormone. Clauberg (O) brought about enlargement of the uterus by injections of follicle hormone and demonstrated the growth by means of beautiful hysterosalpingograms. Werner and Collier (O), by means of theelin, produced changes in the atrophied endometrium of castrated women that approximate the interval changes found in normal women, and they induced bleeding qualitatively indistinguishable from menstruation in normal women. These authors later (A.M.A.) reported an additional study confirming their original report. Hübsher (S.E.G.G.S.) produced menstrual bleeding in an eighty-year-old woman by the administration of follicle and luteal hormones. Haultain (E.O.S.) obtained a cure with follicle hormone in the majority of his cases of amenorrhea, but he does not consider this therapy specific.

Szarka (G.G.S.) administered large doses of follicle hormone to women and produced a condition in the endometrium similar to glandular cystic hyperplasia. Hence here is proof that this condition is due to the excessive action of follicle hormone.

In the treatment of both amenorrhea and uterine bleeding, Anspach and Hoffman (O.S.P.) found that thyroid medication is of service in a considerable proportion of cases and iodine occasionally has a place. Ovarian preparations seem to be of little service but anterior pituitary luteinizing hormone in the treatment of uterine bleeding seems to be effectual in a fair proportion of cases. Stimulation of the anterior pituitary gland with the x-ray is sometimes responsible for a restoration of function. King (A.G.S.) has been disappointed in the use of the luteinizing principle of the anterior pituitary and he emphasized the importance of the thyroid in cases of hyperplasia and dysfunctional bleeding. In cases of menopausal and secondary amenorrhea, Hall (S.S.M.I.) used hormone therapy and obtained results only short of miraculous. Jayle (F.G.C.) advocated the use of folliculin for disturbances of ovarian origin and Stricker (B.O.G.S.) recommended pituitary and corpus luteum hormones for amenorrhea, oligomenorrhea, polymenorrhea, roentgen amenorrhea, the preclimacteric, and the climacteric. Gauss and Buschbeck (G.G.S.) recommended ovarian therapy for the same conditions and also for dysmenorrhea. Likewise Goodall (C.M.A.) favored the use of hormones for these disturbances. Hoevelmann (B.O.G.S.), however, pointed out that amenorrhea is only a symptom and if it is due to tuberculosis, diabetes or other ailments, or if it is the result of the climacterium, folliculin will be of no avail.

Sevringhaus (C.S.C.R.) used genuine anterior pituitary extracts in women with ovarian cystic disease and obtained results of considerable promise including regulation of menstrual rhythm and volume and relief of disturbing symptoms.

Gabrielianz (C.G.S.) believes that the cause of painful breasts lies probably in overactivity of the corpus luteum due to hyperfunction of the anterior pituitary

gland. He cured five out of eight women with mastodynia by means of ovarian residue and two by the use of female sex hormone.

Mayer (O) discussed the hormonal cause of habitual abortion and he recommended serum from healthy pregnant women for these cases. Knaus suggested corpus luteum and de Snoo advocated placental preparations.

According to Lewis (A.G.S.) theelin induces in children with gonorrheal vaginitis a proliferation of the vaginal epithelium which rapidly clears up the discharge and appears to eradicate the gonococci. J. C. Hirst (O.S.P.) found that injections of progynon were followed by a definite increase of bleeding and coagulation times in normal newborns of both sexes, that abnormally long coagulation and bleeding times were corrected by theelin and that ieterus neonatorum appeared to clear up more rapidly than usual under injections of theelin.

Moriwaki (K.G.S.) examined nine preparations of follicle hormone sold on the market and found a distinct variation in their potency. The Council on Pharmacy and Chemistry of the A.M.A. reported on "Estrogenic Substances: Theelin" and summarized its attitude by saying, "It cannot at this time be said that theelin has any specific indication in the treatment of menstrual disturbances." "The anterior pituitary-like and the corpus luteum preparations appear to offer more promise of therapeutic usefulness than the estrogenic preparations." Geiling (A.M.A.) emphasizing the need for conservatism in endocrine therapy and research agreed with the foregoing statements.

*The Menopause.*—One of the chief topics discussed before the Eighth Congress of the Association of Gynecologists and Obstetricians of the French Language was "The Treatment of the Symptoms of Artificial Menopause." Brouha considered the experimental basis of artificial menopause, and Van Cauwenberghe discussed the treatment of menopausal symptoms. The latter maintained that hormonal therapy was effective under the following conditions: if the treatment is begun as soon as possible after the patient leaves the hospital, if the patient is not too young, if small doses are administered during the eight or ten days of each month when the patient would have menstruated, if the injections are given intramuscularly and if in addition to hormonal therapy, the physician adds medical, physical, and psychic treatment.

The third part of the French symposium was devoted to prophylaxis of menopausal symptoms. Lamarque discussed temporary sterilization by means of radiation therapy and concluded that in the present state of our knowledge this procedure is not accurate because it does not enable us to predict whether the desired end will be attained or whether the treatment will lead to permanent amenorrhea. Massabuau and Guibal considered the conservative measures employed to prevent symptoms of artificial change of life. Sixteen individuals participated in the discussion of this symposium and some of the discussers presented papers, the chief topic of which was ovarian grafts.

Barrett (O) and other members of a committee studied the symptoms of the menopause in one thousand women and found that 89.7 per cent of these women carried on their usual occupation without interruption due to menopausal symptoms. The percentage of women free from all symptoms was 15.8. Childbearing in no way influenced the age of the menopause. Stalworth (M.S.M.A.) observed 34 patients with hypertension occurring during the change of life and 58.8 per cent of them gave a definite history of toxemia of pregnancy. Huet (S.M.R.P.) successfully treated the symptoms of the menopause in 33 patients by radiating the hypophysis. Martindale (B.M.A.) analyzed the results of artificial menopause in 620 cases of benign uterine conditions. In the 312 cases where this was accomplished by surgical means, the incidence of cure was 97.8 per cent, in the 203 cases



where x-ray treatment was used, the incidence was 94.2 per cent and of the 45 cases treated with radium only 68 per cent were cured. (Cure signifies relief of symptoms, amenorrhea, and reduction in size of uterus.) Whitehouse (T.A.M.) employs blood-letting with encouraging results for menopausal symptoms. He agrees with Wilson that when hysterectomy is necessary, retention of ovarian tissue may actually be harmful. He argues that if it is true that the symptom-complex of the menopause is the result of unbalanced excess and action of the sex hormone, then it is obvious that rational therapy must be based not upon the administration of more of this substance but rather upon the administration of an antidote. An antidote to estrin is insulin and Whitehouse has used this substance with success in cases of severe menopausal symptoms.

#### UTERINE BLEEDING

One of the chief topics for consideration before the German Gynecological Society was "Gynecological Bleeding." Schroeder opened the discussion by taking up the pathogenesis and diagnosis of these bleedings. He pointed out that the cause of the bleeding in regular menstruation is a recurring cycle of changes, the duration of the flow does not exceed eight days, the amount of the flow depends upon the functional ability of the uterine musculature which is influenced by inflammatory processes and tumors, and the time of the bleeding is determined by changes in the ovary. The shortest menstrual cycle is sixteen days, and if the bleeding persists more than eight days, a cause should be sought. In the cases where the menses last more than eight days, there is a 10 per cent incidence of carcinoma, hence a careful anatomic diagnosis must be made. Most of the abnormal bleedings arise in necrotic areas of a glandular cystic hyperplasia of the endometrium. The etiology of this condition is the persistence of ripe, strongly functioning ovarian follicles. For the second part of the discussion Runge took up the therapy of gynecologic bleeding. He emphasized that an attempt must be made to restore regular menstrual periods. In cases of diminished function of the uterine musculature he advised drugs like ergot and hydrastis for the purpose of producing uterine contractions. Other useful remedies are injections of insulin, calcium, foreign proteins, and the patient's own blood or serum. The patient's general resistance must be built up. In young girls too frequent menses should be treated by the additional use of anterior pituitary and corpus luteum hormones. The most frequent cause of atypical bleeding are myomas. In young women these are best treated by myomectomy, and in women over forty-five, roentgen ray therapy is the procedure of choice. In cases of hyperplasia in women over 45, roentgen ray therapy is likewise indicated. To produce rapid cessation of bleeding in women who are anemic the author recommended atmocausis and insertion of radium into the uterus. Blood transfusions are helpful. Tietze discussed the occurrence of periodic nonmenstrual bleeding due either to ovulation, to early pregnancy or to persistence of a follicle. Hubert's investigations showed that during the menstrual flow there is a strong bactericidal action against anthrax bacilli, and this is lacking in the second half of the menstrual interval. Likewise, clinical experience shows that in healthy women the susceptibility to extragenital infections is less during and after the flow than in the second half of the menstrual interval. Schroeder and Buschbeck constructed a special hysteroscope by means of which they can study the changes which occur in the endometrium during the menstrual cycle. This hysteroscope enables the authors to produce sterilization by coagulating the tubal ostia. By means of an ultraspectroscope, Wehefritz studied the hormones which are found in the different phases of the menstrual cycle, and Hirsch-Hoffman reported his studies on the vegetative nervous system and the ovaries. Likewise Klotz studied the physiology

and pathology of the vegetative nervous system in the small pelvis. The foregoing eight papers aroused an enlivened discussion in which 26 men participated. Of interest was the fact that in women who had their uterus removed, mild menstrual periods can be produced by the implantation of endometrium into the vagina as recommended by Schmid.

Schroeder, Kessler and Tietze (O) presented an analysis of 2,419 cases of irregular bleeding. The chief causes in these cases were endometritis 31.9 per cent, pregnancy disturbances 30.4 per cent, carcinoma 23.3 per cent, glandular hyperplasia 15 per cent, polyps 5.7 per cent, and myomas 5 per cent. In a symposium before the Edinburgh Obstetrical Society, Young, Johnstone, Hendry, Haultain, Herzfeld, Miller and Fahmy reviewed their cases of postmenopausal hemorrhage. Of the total of 937 cases, the causative condition was benign in 56.9 per cent and malignant in 43.1 per cent. The chief causes for all of the cases were carcinoma of the cervix 25.7 per cent, undiagnosed ovarian dysfunction 15.4 per cent, polyp 12.2 per cent, genital prolapse 10.4 per cent, carcinoma of the body of the uterus 9.9 per cent, and fibroids 6.7 per cent. The same material was analyzed by Fahmy before the British Congress of Obstetrics and Gynecology. In a series of 101 cases of bleeding in senile women Schulz (N.G.G.S.) found that the site of the bleeding was in the body of the uterus in 26 instances and carcinoma was present in only 3 of these 26 cases. Bécélère (A.G.O.F.L.) believes that 50 per cent of the women who bleed during the menopause have benign glandular hypertrophy of the endometrium and these are the true hemorrhages of the menopause.

Haden and Singleton (O) point out that abnormalities of menstruation are commonly found in women with simple achlorhydric anemia and respond readily to adequate doses of iron. These authors emphasize that this form of anemia should be suspected in all cases of unexplained menstrual disturbances and the suspicion verified by gastric analysis and blood examination. Jameson (N.Y.O.S.) stated that he has had to curette a number of tuberculous women who had metrorrhagia, and in the large proportion of these cases the pathologist was unable to solve the question of why bleeding occurred. He recalled that tuberculosis exerts a profound effect upon the menstrual cycle. Mayer and also Matthews recommended radiation therapy for the purpose of producing temporary amenorrhea in tuberculous women because during the period of amenorrhea the tuberculous condition improves.

In the opinion of Shaw (B.M.A.) most menstrual irregularities are due to a disturbance in ovarian function although it is impossible to tell whether the majority are primarily ovarian in origin. There are two main deficiencies in our modern treatment, namely the lack of a precise biochemic method for determining abnormal departures in the circulating hormones and the absence of standardized hormones of high concentration. Forster (I.S.M.A.) has no enthusiasm for hormone therapy in cases of functional menstrual disturbances, but Van S. Smith and Rock (O) cured 28 and benefited 22 out of 56 women with dysfunctional bleeding by the administration of extracts of urine of pregnant women. Burch and Burch (C.A.O.G.) likewise obtained good results with these urinary extracts in cases of endometrial hyperplasia. The latter is a disorder of the hypophyseal-ovarian relationship resulting in abnormal declines in the amounts of available estrin and anterior pituitary hormones. Klingler and Burch (O) report an additional case where this therapy was successful.

Witherspoon (O.P.M.S.) presented a preliminary report on the injection of blood from pregnant donors in cases of menstrual disorders but he drew no conclusions. Peck and Goldberger (O) observed good results in these cases with moccasin venom. Mavromati (B.G.S.) administered insulin and obtained excellent results in cases of ovarian meno- and metrorrhagia, good results in dysmenorrhea,

hypo- and oligomenorrhea, and mediocre results in chronic metritis with metrorrhagia. Theilhaber (B.O.G.S.) praised intrauterine diathermy for the treatment of uterine bleeding.

Heynemann (N.W.G.G.S.) discussed the treatment of hemorrhages in the juvenile and recommended drugs to produce uterine contractions, anterior pituitary hormone, corpus luteum hormone, thyroid preparations, curettement, and injections of serum, blood calcium, hypertonic saline solution, Congo red and other substances. He does not believe in radiation therapy. For the treatment of hemorrhages of the menopause Bécèle (A.G.O.F.L.) advocated roentgenotherapy.

For uterine hemorrhage due to persistent ovarian follicles, Yokota (K.G.S.) punctured the follicles through the vagina and obtained brilliant results. In similar cases, Clauberg (O) obtained good results with a single transfusion of a large amount of blood from a pregnant woman.

Much has recently been written on the variability of the menstrual intervals. King (O) added a study of 354 intervals to her former report of 523 and corroborated her previous conclusion on the irregularity of the occurrence of menstruation in normal women. Allen (C.G.S.) found such marked variability in the menstrual function of normal healthy nurses that he insists we should abandon our ideas that normally the periods are regular and at intervals of twenty-eight days. Fluhmann (P.C.S.O.G.) also studied the menstrual cycles in a group of nurses and maintained that the length of successive menstrual cycles in normal women is characterized by marked irregularity in at least two-thirds of instances. Hajek (S.E.G.G.S.) studied 1,480 women and found that only 56.6 per cent had a regular twenty-eight-day cycle and 8.6 per cent had a thirty-day cycle. Kennedy (O) in a study of 10,219 hospital records found that three-fourths of women said they menstruated at twenty-eight-day intervals but data of differences of plus and minus two days were not available.

#### SOCIETIES

1. **A.A.O.G.A.S.**, American Association of Obstetricians, Gynecologists, and Abdominal Surgeons
2. **A.C.P.**, American College of Physicians
3. **A.C.P.T.**, American Congress of Physical Therapy
4. **A.G.O.F.L.**, Association of Gynecologists and Obstetricians of the French Language
5. **A.G.S.**, American Gynecological Society
6. **A.M.A.**, American Medical Association
7. **A.P.H.A.**, American Public Health Association
8. **A.R.S.**, American Radium Society
9. **B.C.O.G.**, British Congress of Obstetrics and Gynecology
10. **B.G.S.**, Bucharest Gynecological Society
11. **B.M.A.**, British Medical Association
12. **B.O.G.S.**, Bavarian Obstetric and Gynecological Society
13. **Br.G.S.**, Brooklyn Gynecological Society
14. **B.S.O.G.**, Berlin Society of Obstetrics and Gynecology
15. **C.A.O.G.**, Central Association of Obstetricians and Gynecologists
16. **C.A.P.S.**, Congress of American Physicians and Surgeons
17. **C.C.A.C.S.**, Clinical Congress of American College of Surgeons
18. **C.S.C.R.**, Central Society for Clinical Research
19. **C.C.M.S.**, Cumberland County Medical Society
20. **C.M.A.**, Canadian Medical Association
21. **C.G.S.**, Chicago Gynecological Society
22. **D.G.S.**, Dresden Gynecological Society
23. **E.O.S.**, Edinburgh Obstetrical Society
24. **F.A.C.C.**, Fourth Australian Cancer Conference
25. **F.G.C.**, French Gynecological Congress
26. **G.G.S.**, German Gynecological Society
27. **G.R.S.**, German Roentgen Society

28. **G.S.B.**, Gynecological Society of Breslau
29. **G.S.S.**, German Surgical Society
30. **H.O.S.**, Hamburg Obstetrical Society
31. **Id.S.M.A.**, Idaho State Medical Association
32. **I.S.M.A.**, Indiana State Medical Association
33. **I.S.M.S.**, Illinois State Medical Society
34. **K.C.H.M.S.**, King's College Hospital Medical School
35. **K.G.S.**, Kinki Gynecological Society (Japan)
36. **L.S.S.**, Lyon Surgical Society
37. **Ma.M.A.**, Maine Medical Association
38. **M.A.M.**, Minnesota Academy of Medicine
39. **M.G.O.G.S.**, Middle German Obstetrical and Gynecological Society
40. **M.M.S.**, Massachusetts Medical Society
41. **M.R.O.G.S.**, Middle Rhine Obstetrical and Gynecological Society
42. **M.S.C.M.S.**, Memphis and Shelby County Medical Society
43. **M.S.M.A.**, Mississippi State Medical Association
44. **N.E.G.G.S.**, North East German Gynecological Society
45. **N.E.G.O.S.**, New England Gynecological and Obstetrical Society
46. **N.G.G.S.**, North German Gynecological Society
47. **N.J.S.M.S.**, New Jersey State Medical Society
48. **N.W.G.G.S.**, Northwest German Gynecological Society
49. **N.Y.A.M.**, New York Academy of Medicine
50. **N.Y.O.S.**, New York Obstetrical Society
51. **N.Y.P.B.O.S.**, New York, Philadelphia and Boston Obstetrical Societies
52. **N.Y.S.M.S.**, New York State Medical Society
53. **O.**, Paper not read before a society
54. **O.P.M.S.**, Orleans Parish Medical Society
55. **O.S.M.S.**, Oregon State Medical Society
56. **O.S.P.**, Obstetrical Society of Philadelphia
57. **P.C.S.O.G.**, Pacific Coast Society of Obstetrics and Gynecology
58. **P.G.M.S.**, Prague German Medical Society
59. **R.A.M.I.**, Royal Academy of Medicine in Ireland
60. **R.S.M.**, Royal Society of Medicine
61. **R.S.N.A.**, Radiological Society of North America
62. **S.D.M.S.**, Seventh District (N. C.) Medical Society
63. **S.E.G.G.S.**, South East German Gynecological Society
64. **S.F.B.C.O.G.S.**, San Francisco Bay Counties Obstetrical and Gynecological Societies
65. **S.G.O.G.S.**, South Germany Obstetrical and Gynecological Society
66. **S.M.A.**, Southern Medical Association
67. **S.M.R.P.**, Society of Medical Radiology of Paris
68. **S.O.G.S.**, Swiss Obstetric and Gynecological Society
69. **S.S.M.I.**, Sacramento Society for Medical Improvement
70. **T.A.M.**, Toronto Academy of Medicine
71. **Te.S.M.A.**, Tennessee State Medical Association
72. **T.S.M.A.**, Tri-State Medical Association
73. **U.C.**, University of Chicago
74. **U.R.O.G.S.**, Upper Rhine Obstetric and Gynecological Society
75. **V.G.O.S.**, Vienna Gynecological and Obstetrical Society
76. **W.D.M.S.**, Watertown District Medical Society

*(To be concluded in September issue.)*

*(Total bibliography to appear in September.)*

# Item

## American Board of Obstetrics and Gynecology

At the examination held in Cleveland, Ohio, on June eleventh and twelfth, sixty-one candidates for certification were examined. Fifty applicants were approved, ten conditioned, and one failed.

The following applicants passed a successful examination and were certified as Diplomates of the American Board of Obstetrics and Gynecology:

### CALIFORNIA

COLEMAN, D. D., Alhambra  
LEWIS, C. H., Santa Monica

### GEORGIA

BARTHOLOMEW, R. A., Atlanta  
SHARPLEY, H. F., Savannah

### ILLINOIS

DAVIS, M. E., Chicago  
PARSONS, ELOISE, Chicago

### KENTUCKY

STARR, S. H., Louisville  
WHITEHOUSE, A. J., Lexington

### LOUISIANA

SELLERS, T. B., New Orleans

### MASSACHUSETTS

DAVIS, MAX, Boston  
O'CONNOR, J. W., Worcester  
ROCK, JOHN, Boston  
ROSENFELD, H. H., Boston  
SHIPTON, G. M., Pittsfield  
TENNEY, BENJAMIN, Boston

### MICHIGAN

MACK, H. C., Detroit  
NELSON, H. M., Detroit

### MISSOURI

VAN DEL, D. T., Kansas City

### NEW JERSEY

NORTON, J. F., Jersey City

### NEW YORK

BARRETT, R. L., New York City  
BARROWS, D. N., New York City  
BLAKELY, S. B., Binghamton  
DER BRUCKE, M. G., Brooklyn  
GLASS, MORRIS, Brooklyn  
HALL, S. C., Brooklyn  
KIERNAN, J. O'C., Albany  
LOCHNER, J. L., Albany  
MAZZOLA, V. P., Brooklyn  
OGINZ, PHILIP, Brooklyn  
POLIFKA, KARL, New York City  
SIEGLER, S. L., Brooklyn

### OHIO

BARNEY, W. R., Cleveland  
BENNETT, A. E., Cleveland  
CANNELL, D. E., Cleveland  
FAULKNER, R. L., Cleveland  
MOWRY, F. S., Cleveland

### OREGON

DUDMAN, V. E., Portland  
HOLMAN, A. W., Portland

### PENNSYLVANIA

BIETSCH, C. F., Pittsburgh  
CARROLL, J. H., Pittsburgh  
CONTI, E. A., Pittsburgh  
EISAMAN, J. R., Pittsburgh  
MOHLER, R. W., Philadelphia  
SCHEFFEY, L. C., Philadelphia  
TRUMPETER, J. H., Beaver

### RHODE ISLAND

MATTEO, F. I., Providence



## SOUTH CAROLINA

McCRADY, R. L., Charleston

## TEXAS

SACHER, C. B., Dallas

## TENNESSEE

LEWIS, M. S., Nashville

## VIRGINIA

THORNHILL, P. E., Norfolk

The next written examination and review of case histories for Group B candidates will be held in various cities in the United States and Canada where there are applicants on Saturday, November 3, 1934.

For further information and application blanks apply to the Secretary, Paul Titus, M.D., 1015 Highland Building, Pittsburgh, Pa.